# Scientific and Technical Information Center

| SEARCH REQUEST FORM   |
|---|
| Requester's Full Name: ABIHH GAZI Examiner #: 74141 Date: 6/12/06  Art Unit: 1616 Phone Number: 2-0622 Serial Number: 10/500 532  |
| Location (Bldg/Room#): (Mailbox #): 4 C To Results Format Preferred (circle): PAPER DISK  |
| To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:   |
| Title of Invention: Process of Pref. of 1-3-(directly formicus) propyl.   |
| HIVEHIOLS THEASE DIOVIGE INITIATIES I.  |
| Earliest Priority Date: 1/7/2002 (371)  |
| Earliest Priority Date: 01/7/2682 (371)   |
| Search Topic:  Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention.  Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. |
| *For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number. 1-3, 5-22, 41-42, 44,45,4 F   |
| . Please search for beings furains of   |
| formula 1, 2  |
| Called as Citalopran  |
| 21 chue Inventor + assigne  |
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| STAFF USE, ONLY Type of Search Vendors and cost where applicable  |
| Searcher: Salon feer NA Sequence (#) STN Dialog   |
| Searcher Phone #: AA Sequence (#) Questel/Orbit Lexis/Nexis   |
| Searcher Location: Structure (#) Westlaw WWW/Internet   |
| Date Searcher Picked Up: 6/19/06 Bibliographic In-house sequence systems  |
| Date Completed: 6/1910 6 Litigation Commercial Oligomer Score/Length Interference SPDI Encode/Transl Other (specify)  |
| Searcher Prep & Review Time: Fulltext   |
| Online Time: 67 min Other   |

PATENT ASSIGNEE(S):

Pharmachem Technologies Limited, UK

SOURCE:

PCT Int. Appl., 55 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                            KIND
                                    DATE
                                            APPLICATION NO.
                                                                            DATE
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      WO 2003029236
                                    20030410
                             A1
                                               WO 2002-EP10645
                                                                            20020923
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               CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
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      US 2003153774
                             A1
                                    20030814
                                                US 2002-242322
      US 6967259
                             B2
                                    20051122
     CA 2461213
                             AΑ
                                    20030410
                                                 CA 2002-2461213
                                                                            20020923
     EP 1430044
                             A1
                                    20040623
                                                 EP 2002-779403
                                                                           20020923
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              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
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                                                                           20051122
PRIORITY APPLN. INFO.:
                                                 US 2001-324821P
                                                                       P 20010924
                                                 US 2002-242322
                                                                        A 20020911
                                                 WO 2002-EP10645
                                                                       W 20020923
OTHER SOURCE(S):
```

CASREACT 138:305791

The present invention provides a process for the preparation of Citalopram, a known antidepressant.

IT 59729-32-7P 59729-33-8P, Citalopram 64169-39-7P RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(process for the preparation of citalogram and derivs.)

RN 59729-32-7 CAPLUS

5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-CN fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

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#### HBr

59729-33-8 CAPLUS RN

5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-СŅ fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN64169-39-7 CAPLUS

1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-CN dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

1

ACCESSION NUMBER:

2003:172971 CAPLUS

DOCUMENT NUMBER:

138:221462

TITLE:

Improved process for the manufacture of citalogram  $% \left( 1\right) =\left( 1\right) \left( 1\right) \left($ 

hydrobromide from 5-bromophthalide

PATENT ASSIGNEE(S):

Sekhsaria Chemicals Ltd., India

SOURCE:

Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

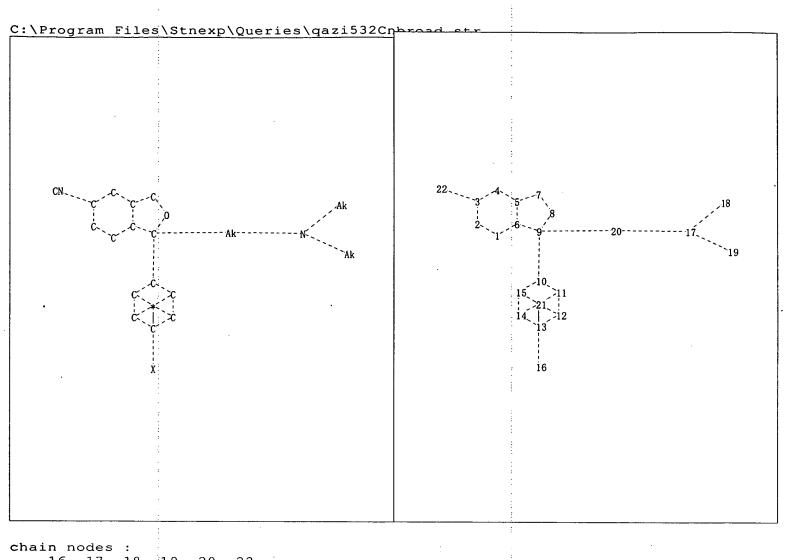
Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

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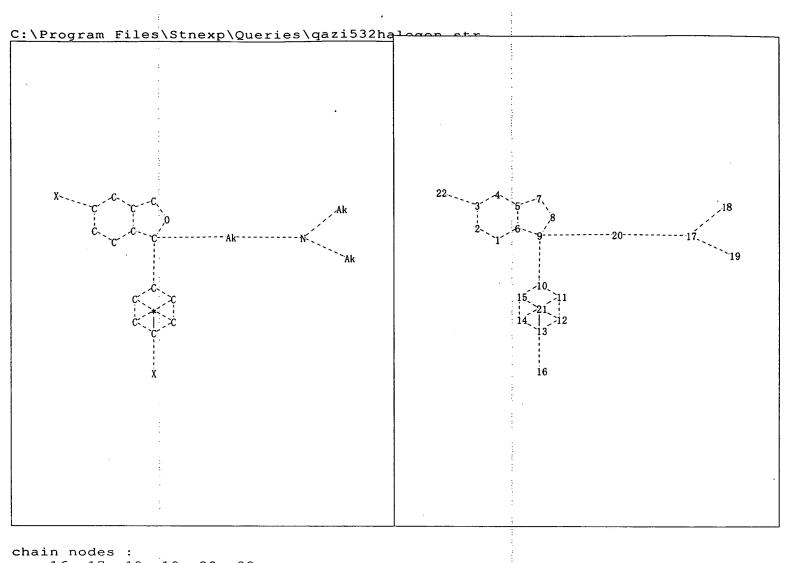
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|------------|------|----------|-----------------|----------|
|            |      |          |                 |          |
| EP 1288211 | A1   | 20030305 | EP 2002-255750  | 20020819 |



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16 17 18 19 20
                     22
ring nodes :
             5
   1 2 3 4
                   7
                 6
                     8
                         9 10 11
                                   12
                                      13 14
                                             15
chain bonds :
   3-22 9-10 9-20 17-19 17-18 17-20
ring bonds :
   1-2 1-6 2-3 3-4 4-5
12-13 13-14 14-15
                         5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12
exact/norm bonds :
   1-2 1-6 2-3 3-4 3-22 4-5 5-6 5-7 6-9 7-8 8-9 9-10 9-20 10-11
   10-15 11-12 12-13 13-14 14-15 17-19 17-18 17-20
Match level:
   1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom
                                                             9:Atom
   10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS
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18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS

17:CLASS

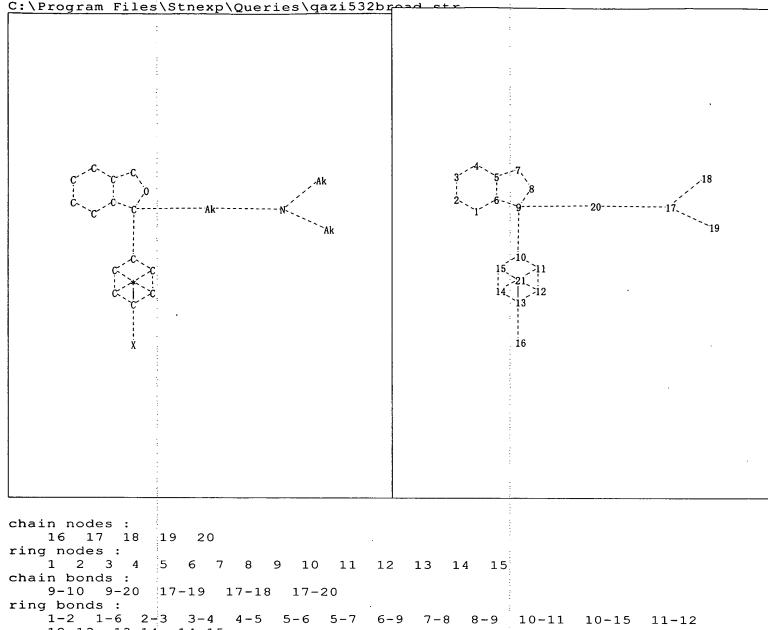


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16 17 18
               19 20
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ring nodes :
   1 2 3 4
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                                               14 15
chain bonds :
               9-20 17-19
    3-22 9-10
                            17-18
ring bonds :
                             5-6
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    1-2 1-6 2-3 3-4 4-5
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    12-13 13-14 14-15
exact/norm bonds :
    1-2 1-6 2-3 3-4 3-22 4-5 5-6 5-7 6-9 7-8 8-9 10-15 11-12 12-13 13-14 14-15 17-19 17-18 17-20
                                                             9-10 9-20 10-11
Match level :
    1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom
    10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS
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Subset (Readont)

18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS

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chain bonds:
 9-10 9-20 17-19 17-18 17-20

ring bonds:
 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12
 12-13 13-14 14-15

exact/norm bonds:
 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-10 9-20 10-11 10-15
 11-12 12-13 13-14 14-15 17-19 17-18 17-20

Match level:
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS

Broad Struct.

18:CLASS 19:CLASS 20:CLASS 21:CLASS

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L10

(FILE 'HOME' ENTERED AT 13:55:54 ON 19 JUN 2006)

FILE 'CAPLUS' ENTERED AT 14:03:44 ON 19 JUN 2006 E US2004-500532/APPS

- L1 1 SEA ABB=ON PLU=ON US2004-500532/AP D BROWSE
  - E RAJAMANNAR T/AU
- L2 21 SEA ABB=ON PLU=ON ("RAJAMANNAR T"/AU OR "RAJAMANNAR THENNATI" /AU)
  - E SRINIVASU K/AU
- L3 6 SEA ABB=ON PLU=ON "SRINIVASU K"/AU E PATEL N/AU
- L4

  184 SEA ABB=ON PLU=ON ("PATEL N"/AU OR "PATEL N S"/AU OR "PATEL

  N S A"/AU OR "PATEL NAME NOT TRANSLATED"/AU OR "PATEL NILESH"/A

  U OR "PATEL NILESHKUMAR"/AU OR "PATEL NILESHKUMAR SURESHBAI"/AU

  OR "PATEL NILESHKUMAR SURESHBHAI"/AU)

  E RAJENDRAN C/AU
- L5 13 SEA ABB=ON PLU=ON ("RAJENDRAN C"/AU OR "RAJENDRAN C P"/AU OR "RAJENDRAN C PANCHAPAKESA"/AU)
- L6 0 SEA ABB=ON PLU=ON (L2 AND (L3 OR L4 OR L5)) OR (L3 AND (L4 OR L5)) OR (L4 AND L5)
- L7 224 SEA ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5)
- L8 1 SEA ABB=ON PLU=ON L7 AND L1 E SUN /CS, PA
- L9 1 SEA ABB=ON PLU=ON ("SUN A PHARM CO LTD"/CS OR "SUN A PHARM CO LTD"/PA OR "SUN A PHARM CO LTD JAPAN"/CS OR "SUN A PHARM CO LTD JAPAN"/PA)
  - E SUN P/CS,PA E SUN PHARM?/CS,PA
  - 434 SEA ABB=ON PLU=ON SUN PHARM?/CS,PA
    - D BIB 3
- L11 0 SEA ABB=ON PLU=ON SUN/OBI (1W) PHARM?/CS,PA
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  - E SUN PHARM/CS,PA
    E SUN PHARM/CS,PA
- L12 96 SEA ABB=ON PLU=ON ("SUN PHARM CORP POMPANO BEACH FL USA"/CS OR "SUN PHARM IND VADODARA 390 007 INDIA"/CS OR "SUN PHARM LTD POMPANO BEACH FL USA"/CS OR "SUN PHARMA ADVANCE RESEARCH CENTER BARODA 390 020 INDIA"/CS OR "SUN PHARMA ADVANCE RESEARCH CENTER VADODARA 390 020 INDIA"/CS OR "SUN PHARMA ADVANCED RES CENT AKOTA GUJARAT INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE AKOTA VADODARA 390020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA 390 020 GJ INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA GUJARAL 390 020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE VADODARA 390020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE VADODARA INDIA"/CS OR "SUN PHARMACEUTICAL CORP"/CS OR "SUN PHARMACEUTICAL CORP"/PA OR "SUN PHARMACEUTICAL CORP USA"/CS OR "SUN PHARMACEUTICAL CORP USA"/PA OR "SUN PHARMACEUTICAL IND LTD"/CS OR "SUN PHARMACEUTICAL IND LTD"/PA OR "SUN PHARMACEUTICAL IND LTD INDIA"/CS OR "SUN PHARMACEUTICAL IND LTD INDIA"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/C S OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED INDIA"/CS OR "SUN PHARMACEUTI CAL INDUSTRIES LIMITED INDIA"/PA OR "SUN PHARMACEUTICAL

Saloni Sharma 06/19/2006

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                   OR "SUN PHARMACEUTICAL INDUSTRIES LTD INDIA"/CS OR "SUN
                   PHARMACEUTICAL INDUSTRIES LTD INDIA"/PA OR "SUN PHARMACEUTICALS
                    ADVANCED RESEARCH CENTRE VADODARA INDIA"/CS OR "SUN PHARMACEUT
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11 SEA ABB=ON PLU=ON L13 AND (L1 OR L2 OR L3 OR L4 OR L5)
T.13
L14
                   E CITALOPRAM/CT
                   E E3+ALL
           1720 SEA ABB=ON PLU=ON CITALOPRAM+PFT/CT
15343 SEA ABB=ON PLU=ON (BENZOFURAN?)/OBI,BI
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3 SEA ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5 OR L13) AND
L15
L16
L17
L18
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FILE 'REGISTRY' ENTERED AT 14:21:48 ON 19 JUN 2006

(L15 OR L16 OR L17)

L19 STRUCTURE UPLOADED

5 SEA SSS SAM L19 L20

D OUE L19

385 SEA SSS FUL L19 L21

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L22

L23

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FILE 'REGISTRY' ENTERED AT 14:28:52 ON 19 JUN 2006

L25 STRUCTURE UPLOADED

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20 SEA SUB=L21 SSS SAM L25 L27

L28 351 SEA SUB=L21 SSS FUL L25

L29 STRUCTURE UPLOADED

L32

L30 11 SEA SUB=L21 SSS SAM L29

L31 207 SEA SUB=L21 SSS FUL L29

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1887 SEA ABB=ON PLU=ON L31

L33 ANALYZE PLU=ON L32 1-1887 RN: 15932 TERMS

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FILE 'CAPLUS' ENTERED AT 14:35:45 ON 19 JUN 2006 1720 SEA ABB=ON PLU=ON L34 L35

FILE 'REGISTRY' ENTERED AT 14:36:52 ON 19 JUN 2006

Saloni Sharma 06/19/2006

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D QUE L25
L36
                STRUCTURE UPLOADED
                STRUCTURE UPLOADED
L37
              1 SEA SUB=L21 SSS SAM L36
L38
                D SCAN
L39
             49 SEA SUB=L21 SSS FUL L36
L40
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L43
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                            PLU=ON
                                   L39 (L) RACT+ALL/RL
L44
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                            PLU=ON
                                   L42 AND L43
L45
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                                    (L44 OR L1)
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                D SCAN
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L47
L48
             15 SEA SSS FUL L37
                SEL L47 BRN
              2 SEA ABB=ON PLU=ON (1393707/RX.RBRN OR 1393708/RX.RBRN OR
L49
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                SEL BRN L48
L*** DEL
             15 S E10-E24
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L50
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                9001443/RX.PBRN OR 9001444/RX.PBRN OR 9826316/RX.PBRN OR
                9826317/RX.PBRN)
L51
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                                    L49 AND L50
L52
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     FILE 'BEILSTEIN' ENTERED AT 14:55:39 ON 19 JUN 2006
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L53
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L54
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                           PLU=ON L45 NOT (PY>2002 OR PRY>2002 OR AY>2002)
L55
           1824 SEA ABB=ON PLU=ON L32 AND (L15 OR L16 OR L17)
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FILE 'CAPLUS' ENTERED AT 15:01:02 ON 19 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 19 Jun 2006 VOL 144 ISS 26 FILE LAST UPDATED: 18 Jun 2006 (20060618/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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| L12      | 96  | SEA FILE=CAPLUS ABB=ON PLU=ON ("SUN PHARM CORP POMPANO BEACH  |
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|          |     | "SUN PHARM LTD POMPANO BEACH FL USA"/CS OR "SUN PHARMA ADVANCE  |
|          |     | RESEARCH CENTER BARODA 390 020 INDIA"/CS OR "SUN PHARMA   |
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|          |     | IND LTD INDIA"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/C<br>S OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/PA OR "SUN |
|          |     | PHARMACEUTICAL INDUSTRIES LIMITED "/PA OR "SUN PHARMACEUTI  |
|          |     | CAL INDUSTRIES LIMITED INDIA"/PA OR "SUN PHARMACEUTICAL   |
|          |     | INDUSTRIES LIMITED INDIA"/PA OR "SON PHARMACEUTICAL INDUSTRIES LTD"/PA  |
|          |     | OR "SUN PHARMACEUTICAL INDUSTRIES LTD INDIA"/CS OR "SUN   |
|          |     | PHARMACEUTICAL INDUSTRIES LID INDIA"/CS OR "SUN PHARMACEUTICALS   |
|          |     | ADVANCED RESEARCH CENTRE VADODARA INDIA"/CS OR "SUN PHARMACEUT  |
|          |     | ICALS CORPORATION"/CS OR "SUN PHARMACEUTICALS CORPORATION"/PA   |
|          |     | OR "SUN PHARMACEUTICALS CORPORATION USA"/CS OR "SUN PHARMACEUTI   |
|          |     | OR SON FRANCEUTICALS CORPORATION USA / CS OR SON PRARMACEUTI  |

Saloni Sharma 06/19/2006

S INDUSTRIES LTD INDIA"/PA)

CALS CORPORATION USA"/PA OR "SUN PHARMACEUTICALS INDUSTRIES LTD"/CS OR "SUN PHARMACEUTICALS INDUSTRIES LTD"/PA OR "SUN PHARMACEUTICALS INDUSTRIES LTD INDIA"/CS OR "SUN PHARMACEUTICAL

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L13
             96 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                               L10 AND L12
L14
             11 SEA FILE=CAPLUS ABB=ON PLU=ON
                                               L13 AND (L1 OR L2 OR L3 OR L4
L15
          1720 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                CITALOPRAM+PFT/CT
          15343 SEA FILE=CAPLUS ABB=ON
1.16
                                        PLU=ON
                                                (BENZOFURAN?) / OBI, BI
L17
          2355 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                (CITALOPRAM?) / OBI, BI
L18
              3 SEA FILE=CAPLUS ABB=ON
                                       PLU=ON
                                                (L1 OR L2 OR L3 OR L4 OR L5 OR
                L13) AND (L15 OR L16 OR L17)
L53
            12 SEA FILE=CAPLUS ABB=ON PLU=ON
                                                (L14 OR L18)
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L53 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
                         2006:380769 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         144:412891
TITLE:
                         Preparation of aminocycloalkanedicarboxylic acids and
                         related compounds as immunosuppressive agents
INVENTOR(S):
                         Capet, Marc; Levoin, Nicolas; Berrebi-Bertrand,
                         Isabelle; Poupardin, Olivia; Robert, Philippe;
                         Schwartz, Jean-Charles; Lecomte, Jeanne-Marie;
                         Rajamannar, Thennati; Pal, Ranjan Kumar;
                         Samanta, Biswajit; Jivani, Jignesh K.; Panchal,
                         Bhavesh M.; Bhatt, Isha H.; Aradhye, Jayraj D.
PATENT ASSIGNEE(S):
                         Bioprojet, Fr.; Sun Pharmaceuticals Industries
                         Ltd.
SOURCE:
                         Eur. Pat. Appl., 39 pp.
                         CODEN: EPXXDW
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                        KIND
     PATENT NO.
                                           APPLICATION NO.
                               DATE
                                                                   DATE
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                        _ _ _ _
                               -----
                                           _______
                                                                   -----
     EP 1650186
                               20060426
                                         EP 2004-292517
                         A1
                                                                   20041022
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
     WO 2006043149
                               20060427
                                           WO 2005-IB3113
                         A2
                                                                   20051018
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
            NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
            SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
            YU, ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:
                                            EP 2004-292517
                                                                A 20041022
     The invention relates to amino dicarboxylic acid derivs.
     Ar1-Y10-1-X0-1-Ar20-1-Y2-NR'-Y30-1-Z(CO2R'')COR''' [Ar1, Ar2 are
```

Ar1-Y10-1-X0-1-Ar20-1-Y2-NR'-Y30-1-Z(CO2R'')COR''' [Ar1, Ar2 are (un)substituted aryl; Y1, Y2, Y3 are (un)substituted alkyl chains; X is a heteroatom; R', R'' are independently H or an (un)substituted alkyl chain; R''' is OH, alkoxy, H, an amino group, a natural or synthetic amino acid; Z is cycloalkyl, heterocyclyl, aryl, heteroaryl, CH, C-alkyl or Z and R' may form a ring; CO2R'' and COR''' are attached to the same atom or

Saloni Sharma 06/19/2006

adjacent atoms] which display agonistic activity at sphingosine-1-phosphate (S1P) receptors for use as immunosuppressive agents. Thus, 3-(4-nonylbenzylamino)cyclopentane-1,1-dicarboxylic acid was prepared and shown to activate the S1P1 receptor (EC50 = 6) nM.

REFERENCE COUNT:

THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

22

ACCESSION NUMBER:

2006:194068 CAPLUS

DOCUMENT NUMBER:

144:274127

TITLE:

Process for preparation of citalogram and

its enantiomers via acid or base cyclization of the

diol

INVENTOR(S):

Periyandi, Nagarajan; Kilaru, Srinivasu; Thennati,

Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Limited, India

SOURCE:

PCT Int. Appl., 31 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

GI

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATEN      | T NO.   |     |     | KIN  | D   | DATE |      | 7   | APPL | ICAT  | ION 1 | . 00 |     | D   | ATE           |     |
|------------|---------|-----|-----|------|-----|------|------|-----|------|-------|-------|------|-----|-----|---------------|-----|
|            |         |     |     |      | -   |      |      |     |      |       |       |      |     | -   |               |     |
| WO 20      | 060219  | 71  |     | A2   |     | 2006 | 0302 | 1   | WO 2 | 005-  | IN27  | 5    |     | 21  | <b>3050</b> 8 | 312 |
| W          | : AE,   | AG, | AL, | AM,  | ΑT, | AU,  | ΑZ,  | BA, | BB,  | BG,   | BR,   | BW,  | BY, | BZ, | CA,           | CH, |
|            | CN,     | CO, | CR, | CU,  | CZ, | DE,  | DK,  | DM, | DZ,  | EC,   | EE,   | EG,  | ES, | FI, | GB,           | GD, |
|            |         | GH, |     |      |     |      |      |     |      |       |       |      |     |     |               |     |
|            | LC,     | LK, | LR, | LS,  | LT, | LU,  | LV,  | MA, | MD,  | MG,   | MK,   | MN,  | MW, | MX, | MZ,           | NA, |
|            |         | NI, |     |      |     |      |      |     |      |       |       |      |     |     |               |     |
|            | -       | SM, |     | -    |     |      |      |     |      | •     |       |      | •   |     | •             |     |
|            | -       | ZM. | -   | •    | •   | ,    | •    | •   | •    | ,     | ,     | •    |     | ,   | ,             | ,   |
| R          | W: AT,  | BE. | BG. | CH.  | CY. | CZ.  | DE.  | DK. | EE.  | ES.   | FT.   | FR.  | GB. | GR. | HU.           | TE. |
|            |         | IT, |     | •    |     | •    | •    |     | •    | •     | •     | •    | •   | •   | ,             |     |
|            |         | CG, |     |      |     |      | -    |     | •    |       | •     |      | -   |     | •             | •   |
|            |         | KE, |     |      |     |      |      |     |      |       |       |      |     |     |               |     |
|            | -       | KZ, | -   |      |     | -    | υ,   | 22, | UL,  | 10,   | 00,   | ,    | 2,  | ,   | 110,          | 21, |
| PRIORITY A | •       | ,   | •   | 100, | 10, | 111  |      |     | IN 2 | 004-1 | MU91: | 2    | ;   | A 2 | 0040          | 823 |
| OTHER SOUR | RCE(S): |     |     | MAR  | TAG | 144: | 2741 | 27  |      |       |       |      |     |     |               | -   |

Z Me N Me F

II

AB The invention provides a process for preparation of 1-[3-(dimethylamino)propyl]-

1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile I (Z = CN; citalopram) and its enantiomers. The process for preparation of compound I comprising reacting a compound of formula II (R = H), in the presence of a base, with a compound of formula RX, wherein R is (un) substituted alkyl, (un) substituted alkenyl, and (un) substituted (hetero) aryl; X is from F, Cl, Br, I, CN, OTf and OR1; R1 is (un) substituted alkyl; Z is CN or a group that may be converted to a cyano group; so that an intermediate ether derivative, where R is as defined above, is formed from said reaction, which ether cyclizes to give a compound of formula I, where Z is not a cyano group, and conversion of the group Z in the compound of formula I to a cyano group to form racemic I (Z = CN), is claimed in this invention. invention also provides ether compds., compds. of formula II and a process for preparation thereof. (S)-(+)-Citropram, i.e., (S)-(+)-I (Z = CN) was prepared by nucleophilic aromatic substitution of 2,5-dichloronitrobenzene with (S)-(-)-II (Z = CN; R = H) to give the corresponding benzylic Ph ether, that was converted to its HCl salt, and cyclized in the presence of potassium carbonate to give (S)-(+)-I.

L53 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:1355587 CAPLUS

DOCUMENT NUMBER:

144:74891

TITLE:

Novel stable polymorphic forms of tiagabine

hydrochloride

INVENTOR(S):

Natarajan, Muthukumaran; Patel, Nileshkumar

Sureshbhai; Bhatt, Mehul Chandrakatbhai; Kilaru,

Srinivasu; Thennati, Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT | NO.                       |     |     | KIN                    | D : | DATE |     | ;   | APPL | ICAT | ION 1 | . 01 |     | D   | ATE |     |    |
|--------|---------------------------|-----|-----|------------------------|-----|------|-----|-----|------|------|-------|------|-----|-----|-----|-----|----|
| WO 200 | WO 2005122698 A2 20051229 |     | 1   | WO 2004-IN447 20041224 |     |      | 224 |     |      |      |       |      |     |     |     |     |    |
| W :    | ΑE,                       | AG, | AL, | AM,                    | ΑT, | AU,  | ΑZ, | BA, | BB,  | BG,  | BR,   | BW,  | BY, | ΒZ, | CA, | CH, |    |
|        | CN,                       | CO, | CR, | CU,                    | CZ, | DE,  | DK, | DM, | DZ,  | EC,  | EE,   | EG,  | ES, | FI, | GB, | GD, |    |
|        | GE,                       | GH, | GM, | HR,                    | HU, | ID,  | IL, | IN, | IS,  | JP,  | ΚE,   | KG,  | ΚP, | KR, | KZ, | LC, |    |
|        | LK,                       | LR, | LS, | LT,                    | LU, | LV,  | MA, | MD, | MG,  | MK,  | MN,   | MW,  | MX, | MZ, | NA, | NI, |    |
|        | NO,                       | NZ, | OM, | PG,                    | PH, | PL,  | PT, | RO, | RU,  | SC,  | SD,   | SE,  | SG, | SK, | SL, | SM, |    |
|        | SY,                       | ТJ, | TM, | TN,                    | TR, | TT,  | TZ, | UA, | UG,  | US,  | UΖ,   | VC,  | VN, | YU, | ZA, | ZM, | ZW |
| RW     | BW,                       | GH, | GM, | KE,                    | LS, | MW,  | MZ, | NA, | SD,  | SL,  | SZ,   | TZ,  | UG, | ZM, | ZW, | ΑM, |    |
|        | ΑZ,                       | BY, | KG, | KZ,                    | MD, | RU,  | ТJ, | TM, | AT,  | BE,  | BG,   | CH,  | CY, | CZ, | DE, | DK, |    |
|        | EE,                       | ES, | FI, | FR,                    | GB, | GR,  | HU, | ΙE, | IS,  | IT,  | LT,   | LU,  | MC, | NL, | PL, | PT, |    |
|        | RO,                       | SE, | SI, | SK,                    | TR, | BF,  | ВJ, | CF, | CG,  | CI,  | CM,   | GA,  | GN, | GQ, | GW, | ΜL, |    |
|        | MR,                       | NE, | SN, | TD,                    | TG  |      |     |     |      |      |       |      |     |     |     |     |    |

PRIORITY APPLN. INFO.:

IN 2003-MU1210

A 20031224

AB Stable polymorphic forms III, IV and substantially amorphous forms of an anticonvulsant, tiagabine-HCl. Thus, a monoacetonitrile solvate of tiagabine-HCl was prepared by the reaction of the drug hydrochloride with

MeCN. The solvate was characterized by x-ray diffraction.

L53 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:294515 CAPLUS

DOCUMENT NUMBER:

142:316575

TITLE:

A process for the preparation of iopamidol in a

pharmaceutically acceptable form

INVENTOR(S): Rajeev, Rehani; Rajamannar, Thennati; Patel,

S. Kartik; Arun, Yadav; Mukesh, Vaghela

PATENT ASSIGNEE(S):

Sun Pharmaceutical Ind. Ltd., India

SOURCE:

Indian, 13 pp. CODEN: INXXAP

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT NO.

English

PATENT INFORMATION:

| KIND     | DATE | APPLICATION NO. | DATE |
|----------|------|-----------------|------|
| <b>-</b> |      |                 |      |

IN 186589

20011006

IN 1999-B0654 19990917

PRIORITY APPLN. INFO.:

IN 1999-B0654 19990917

OTHER SOURCE(S):

CASREACT 142:316575; MARPAT 142:316575

GI

A facile process is described for the preparation of iopamidol I, a non-ionic AB X-ray contrast medium. The process comprises of treatment of an aqueous solution

acetoxyiopamidol II [R = alkyl] with one or more of amine bases, and crystallization of iopamidol directly from the reaction mixture using alc. solvents

to furnish a pharmaceutically acceptable purified iopamidol. Thus, reacting L-5-α-acetoxypropionylamino-2,4,6-triiodoisophthalic acid di(1,3-dihydroxyisopropylamide) with MeNH2 in H2O for 5 h at room temperature followed by addition of 2-propanol and heating to 90°C until complete crystallization, afforded 67% iopamidol (US Pharmacopoeial grade).

L53 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2005:207867 CAPLUS

DOCUMENT NUMBER:

142:246293

TITLE:

A process for the preparation of substantially pure

APPLICATION NO.

DATE

gabapentin

INVENTOR(S): PATENT ASSIGNEE(S): Rajamannar, Thennati; Rajeev, Rehani Sun Pharmaceutical Industries Ltd., India

SOURCE:

Indian, 16 pp. CODEN: INXXAP

DATE

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

KIND

PATENT INFORMATION:

PATENT NO.

| Α             | 20020817   | IN 2000-MU62  | 20000120                 |
|---------------|--|---|--------------------------|
| A             | 20031122   | IN 2001-MU863   | 20010910                 |
| •             |  |   | A 20000120               |
|               |  |   |                          |
| etic acid (ga | abapentin) :   | is described. The p   | rocess comprises         |
| (a) treating  | crude gabaj  | pentin with an alkal  | i such that the pH       |
| on mixture is | s at least '   | 7.5, heating the rea  | ction mixture to a       |
|               |  |   |                          |
| traction int  | to an organ:   | ic solvent followed   | by isolation of          |
|               |  |   |                          |
|               |  |   |                          |
| zation of the | ne salt with   | h a base to precipit  | ate gabapentin, and      |
| recipitated   | gabapentin   |   |                          |
|               | A FO.: the preparatetic acid (ga (a) treating on mixture is at least al attraction into pure gabaper pure gabaper Lzation of the | A 20031122 FO.: the preparation of subsetic acid (gabapentin) (a) treating crude gabapen mixture is at least about 80° and attraction into an organ pure gabapentin-lactam pure gabapentin-lactam zation of the salt with | A 20031122 IN 2001-MU863 |

L53 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:1079731 CAPLUS

DOCUMENT NUMBER:

142:56160

TITLE:

process for purification of citalogram by

hydrogenolysis halogenated isobenzofuran impurities

INVENTOR(S):

Borase, Ashok Punju; Patel, Nileshkumar Sureshbai; Kilaru, Srinivasu; Thennati,

Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceuticals Industries Ltd., India

SOURCE: Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO.             | KIND DATE        | APPLICATION NO.     | DATE            |
|------------------------|------------------|---------------------|-----------------|
|                        |                  |                     |                 |
| EP 1486492             | A2 20041215      | EP 2004-291424      | 20040608        |
| EP 1486492             | A3 20050223      |                     |                 |
| R: AT, BE, CH,         | DE, DK, ES, FR,  | GB, GR, IT, LI, LU, | NL, SE, MC, PT, |
|                        |                  | CY, AL, TR, BG, CZ, |                 |
| US 2005004380          | A1 20050106      | US 2004-865139      | 20040608        |
| US 7019153             | B2 20060328      |                     |                 |
| PRIORITY APPLN. INFO.: |                  | IN 2003-MU602       | A 20030610      |
| OTHER SOURCE(S):       | MARPAT 142:56160 | )                   |                 |
| GI                     |                  |                     |                 |

The present invention provides a process for decreasing the content of AB halogenated isobenzofuran impurities I (X = halo) in citalogram (II) by hydrogenolysis to I (X = H). Thus, 5 g crude citalogram base containing 4.84% of bromo impurity I (X = Br) is dissolved in 50 mL EtOAc, 0.1 g Pd/C and 0.1 g sodium hypophosphite added and the mixture refluxed for 2 h. Anal. showed that the bromo impurity I (X = Br) is absent.

L53 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

2004:832438 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

141:297645

A process for the isolation of pure TITLE:

> 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition salt by neutralization

with base

Gurunath, Gaonkar Subhash; Rajamannar, INVENTOR(S):

Thennati; Shrivastava, Ratnesh

Sun Pharmaceutical Industries Ltd., India PATENT ASSIGNEE(S):

SOURCE: Indian, 10 pp. CODEN: INXXAP

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

AB

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
|                        |      |          |                 |          |
| IN 186285              | Α    | 20010728 | IN 2000-MU76    | 20000124 |
| PRIORITY APPLN. INFO.: |      |          | IN 2000-MU76    | 20000124 |

A process is described for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid (i.e., gabapentin) from an aqueous solution containing acid addition salt of 1-(aminomethyl)cyclohexaneacetic acid [e.g., 1-(aminomethyl)cyclohexaneacetic acid hydrochloride] by treatment with a base (e.g., sodium hydroxide) to the isoelec. point. The process yields pure 1-(aminomethyl)cyclohexaneacetic acid directly from the aqueous solution containing its acid addition salt, which salt is generated during the synthesis of 1-(aminomethyl)cyclohexaneacetic acid by the acid hydrolysis of its corresponding lactam.

L53 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:825284 CAPLUS

DOCUMENT NUMBER: 141:295724

TITLE: A process for the synthesis of 1-(2-nitroaryl)-2-

arylethanes and their substituted derivatives as key intermediates for the production of pharmaceutically CODEN: INXXAP

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. PATENT NO. KIND DATE DATE -----\_ \_ \_ \_ \_\_\_\_\_ \_\_\_\_\_\_ \_ \_ \_ \_ \_ \_ \_ Α IN 182116 19990102 IN 1996-B0362 19960712 PRIORITY APPLN. INFO.: IN 1996-B0362 19960712 GI

A process is described for the recovery of tramadol in the form of AB cis-tramadol hydrochloride, an analgesic drug I.HCl (no biol. data), from trans-tramadol hydrochloride II.HCl, or from a mixture of the diastereomeric cis- and trans-tramadols. The said process comprises isomerization of trans/cis, trans-tramadols under solvolytic conditions by catalysis with an appropriate acid resulting in enrichment of the cis-tramadol component which is then isolated as a pure isomer by crystallization This process when carried out in an iterative manner enables the recovery as cis-tramadol, in asymptotically quant. amts., from trans/cis, trans-tramadols.

L53 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:410231 CAPLUS

DOCUMENT NUMBER:

140:375168

TITLE:

A process for the preparation of 1-(2,3-epoxypropyl)-5nitroimidazoles via condensation of 5-nitroimidazoles

and epichlorohydrin

INVENTOR(S):

Rao, C. Trinadha; Rajamannar, T.; Acharyulu,

P. V. R.; Rehani, R.; Desouza, N. J.

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Ltd., India

SOURCE:

Indian, 26 pp.

CODEN: INXXAP

DOCUMENT TYPE: LANGUAGE:

Patent

FAMILY ACC. NUM. COUNT:

English

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE 19980620 IN 181460 Α IN 1996-B0597 19961210 PRIORITY APPLN. INFO.: IN 1996-B0597 19961210

OTHER SOURCE(S):

CASREACT 140:375168; MARPAT 140:375168

GΙ

active compounds

INVENTOR (S): Rajamannar, T.; De Souza, N. J.

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Ltd., India

SOURCE: 4 Indian, 27 pp.

CODEN: INXXAP

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE ---------------IN 181826 19981003 IN 1995-B0491 19951121 PRIORITY APPLN. INFO.: IN 1995-B0491 19951121 OTHER SOURCE(S):

Ι

CASREACT 141:295724; MARPAT 141:295724

GΙ

$$R^{1}$$
 $CO_{2}R$ 
 $CO_{2}R$ 
 $R^{2}$ 
 $R^{2}$ 
 $R^{4}$ 
 $R^{4}$ 
 $R^{2}$ 
 $R^{2}$ 

AB A new process for the preparation of substituted 1,2-diarylethane derivs. I [X = H, halogens such as Cl, Br and I, and NO2; R1, R4 = H, usual aromatic substituent such as Cl, CH3, OCH3, CF3, NH2 and nitrogen heterocyclic residues; R2 = H, alkyl, (un) substituted aryl; R3 = H, CO2R (wherein R = H, alkyl)] which are key intermediates for the preparation of the well known tricyclic antidepressant drugs, such as clomipramine, imipramine, desipramine, lofepramine and trimipramine, is disclosed. The compds. I are produced by treating the compds. II [R1 is as defined above; R = alkyl] with compound III [R2, R4, X are as defined above; Y = a leaving group such as halo, OMs, OTs] followed by the work-up procedure. Twelve compds. I [R1 = 4-Cl; R2, R4 = H; R3 = CO2Me, CO2H, H] were prepared

L53 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:825283 CAPLUS

DOCUMENT NUMBER: 141:277348

TITLE: A process for the recovery of tramadol as cis-tramadol

hydrochloride in asymptotically quantitative amounts

from mixtures of diastereomers of tramadol

INVENTOR (S): Rajamannar, T.; Rao, Trinadha C.; Sebastian,

Sonny; De Souza, N. J.

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Ltd., India

SOURCE: Indian, 22 pp.

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WO 2003057132
                                20040415
                          C1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                          A1
                                20030724
                                            AU 2003-222435
                                                                    20030107
     AU 2003222435
                                20050224
     US 2005043550
                          Α1
                                            US 2004-500532
                                                                    20040719 <--
                                            IN 2002-MU10
                                                                A 20020107
PRIORITY APPLN. INFO.:
                                            IN 2002-MU18
                                                                A 20020110
                                            IN 2002-MU847
                                                                A 20020930
                                            WO 2003-IN6
                                                                W 20030107
                         CASREACT 139:117333; MARPAT 139:117333
OTHER SOURCE(S):
```

OTHER SOURCE(S):

O.I.

AB Title compound (I; R = cyano) (citalopram) was prepared by treatment of I (R = Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. The PhMe layer was separated and the pH of the aqueous layer was adjusted to 9.0-9.5

with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and

0.23% of the amide and desmethylcitalopram resp.

L53 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

Ι

ACCESSION NUMBER:

2001:699013 CAPLUS

DOCUMENT NUMBER:

135:226785

TITLE:

Etherification and salification process for the industrial-scale manufacture of fluvoxamine maleate

INVENTOR(S):

Chitturi, Rao; Rajamannar, Thennati; Jadav, Kanaksinh Jesingbhai; Shah, Hemant Ashvinbhai

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Ltd., India

$$\mathbb{R}^{2}$$
 $\mathbb{N}$ 
 $\mathbb{R}^{3}$ 

A process for the preparation of 1-(2,3-epoxypropyl)-5-nitroimidazoles I [ R1, AB R2 = NO2, H, halo; R3 = H, halo, alkyl] via the regionelective N-alkylation of 5-nitroimidazoles II by epichlorohydrin in the presence of AlCl3 was provided. For example, to a suspension of 2-methyl-5nitroimidazole (250 g) in Et acetate (2.5 L) under N2 atmosphere was added dropwise anhydrous AlCl3 (328 g), while maintaining the reaction temperature between -10 to -5 °C. Epichlorohydrin (273 g) was then added to the mixture over a 4-h period and the reaction stirred for addnl. 6-h at -10 to -5 °C. After aqueous work-up and treatment with NaOH, 1-(2,3-epoxypropyl)-2-methyl-5-nitroimidazole was obtained in 75% yield. Of note, the use of a Lewis acid instead of a base, as in the prior art, afforded exclusive formation of the 5-nitroimidazole derivative

L53 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:551309 CAPLUS

DOCUMENT NUMBER: 139:117333

TITLE: Process for the preparation of 1-[3-

(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-

5-isobenzofurancarbonitrile via cyanation of the

corresponding chloride or bromide precursors.

INVENTOR(S): Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai,

Rajendran; Patel, Nileshkumar Sureshbhai

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

PCT Int. Appl., 41 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
|               |      |          |                 |          |
| WO 2003057132 | A2   | 20030717 | WO 2003-IN6     | 20030107 |
| WO 2003057132 | A3   | 20040226 |                 |          |

SOURCE: Patentschrift (Switz.), 6 pp.

CODEN: SWXXAS

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

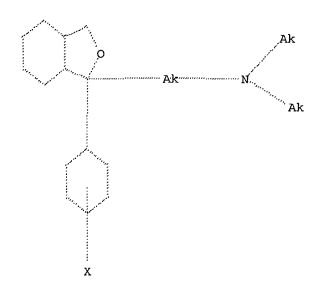
| PATENT NO.      | KIND   | DATE     | APPLICATION NO. |   | DATE     |  |  |
|-----------------|--------|----------|-----------------|---|----------|--|--|
|                 |        |          |                 |   |          |  |  |
| CH 691124       | A      | 20010430 | CH 2000-2194    |   | 20001111 |  |  |
| IN 186677       | A      | 20011020 | IN 1999-BO796   |   | 19991112 |  |  |
| US 6433225      | B1     | 20020813 | US 2000-696613  |   | 20001025 |  |  |
| IT 1319242      | B1     | 20030926 | IT 2000-MI2324  |   | 20001026 |  |  |
| BE 1012819      | A6     | 20010306 | BE 2000-717     |   | 20001110 |  |  |
| PRIORITY APPLN. | INFO.: |          | IN 1999-B0796   | Α | 19991112 |  |  |

OTHER SOURCE(S): CASREACT 135:226785

Fluvoxamine maleate is prepared on an industrial scale by the etherification 5-methoxy-4'-trifluoromethylvalerophenone oxime with 2-chloroethylamine hydrochloride in the presence of bases (e.g., potassium hydroxide) and polyether catalysts (e.g., polyethylene glycol) yielding fluvoxamine which is then salified with maleic acid.

=> d que 145

L11 SEA FILE=CAPLUS ABB=ON PLU=ON US2004-500532/AP L19



Structure attributes must be viewed using STN Express query preparation.

L21 385 SEA FILE=REGISTRY SSS FUL L19

L36 STR

Structure attributes must be viewed using STN Express query preparation. L37 STR

Structure attributes must be viewed using STN Express query preparation.

| L39 | 49  | SEA | FILE=REGIST | RY SUB=L2 | 21 SSS F | UL L36  |             |
|-----|-----|-----|-------------|-----------|----------|---------|-------------|
| L41 | 180 | SEA | FILE=REGIST | RY SUB=L2 | 21 SSS F | UL L37  |             |
| L42 | 115 | SEA | FILE=CAPLUS | ABB=ON    | PLU=ON   | L41 (L) | PREP+ALL/RL |
| L43 | 26  | SEA | FILE=CAPLUS | ABB=ON    | PLU=ON   | L39 (L) | RACT+ALL/RL |
| L44 | 25  | SEA | FILE=CAPLUS | ABB=ON    | PLU=ON   | L42 AND | L43         |
| L45 | 25  | SEA | FILE=CAPLUS | ABB=ON    | PLU=ON   | (L44 OR | L1)         |

=> d ibib abs hitstr 145 tot

L45 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2006:213262 CAPLUS

DOCUMENT NUMBER:

144:292567

TITLE:

Process for preparation of escitalopram

INVENTOR(S):

Pulla Reddy, Muddasani; Sambasiva Rao, Talasila;

Venkaiah Chowdary, Nannapaneni

PATENT ASSIGNEE(S):

Natco Pharma Limited, India

SOURCE:

PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO.    |     |     |     | KIND  |     | DATE     |     |     | APPLICATION NO. |     |     |     |          | DATE |     |     |  |
|---------------|-----|-----|-----|-------|-----|----------|-----|-----|-----------------|-----|-----|-----|----------|------|-----|-----|--|
|               |     |     |     |       |     |          |     |     |                 |     |     |     |          |      |     |     |  |
| WO 2006025071 |     |     |     | A1 20 |     | 20060309 |     | 1   | WO 2005-IN282   |     |     |     | 20050823 |      |     |     |  |
| W :           | ΑE, | AG, | AL, | AM,   | AT, | AU,      | ΑZ, | BA, | BB,             | BG, | BR, | BW, | BY,      | ΒZ,  | CA, | CH, |  |
|               | CN, | CO, | CR, | CU,   | CZ, | DE,      | DK, | DM, | DZ,             | EC, | EE, | EG, | ES,      | FI,  | GB, | GD, |  |
|               | GE, | GH, | GM, | HR,   | HU, | ID,      | IL, | IN, | IS,             | JP, | KE, | KG, | KM,      | KΡ,  | KR, | KZ, |  |
|               | LC, | LK, | LR, | LS,   | LT, | LU,      | LV, | MA, | MD,             | MG, | MK, | MN, | MW,      | MX,  | MZ, | NA, |  |
|               | NG, | NI, | NO, | NZ,   | OM, | PG,      | PH, | PL, | PT,             | RO, | RU, | SC, | SD,      | SE,  | SG, | SK, |  |
|               | SL, | SM, | SY, | ТJ,   | TM, | TN,      | TR, | TT, | ΤZ,             | UA, | UG, | US, | UΖ,      | VC,  | VN, | YU, |  |
|               | ZA, | ZM, | zw  |       |     |          |     |     |                 |     |     |     |          |      |     |     |  |
| RW:           | AT, | BE, | BG, | CH,   | CY, | CZ,      | DE, | DK, | EE,             | ES, | FI, | FR, | GB,      | GR,  | HU, | ΙE, |  |
|               | IS, | ΙΤ, | LT, | LU,   | LV, | MC,      | ΝL, | PL, | PT,             | RO, | SE, | SI, | SK,      | TR,  | BF, | ВJ, |  |
|               | CF, | CG, | CI, | CM,   | GA, | GN,      | GQ, | GW, | ML,             | MR, | ΝE, | SN, | TD,      | TG,  | BW, | GH, |  |
|               | GM, | ΚE, | LS, | MW,   | MZ, | NA,      | SD, | SL, | SZ,             | ΤZ, | UG, | ZM, | ZW,      | AM,  | ΑZ, | BY, |  |
|               | KG, | ΚŻ, | MD, | RU,   | TJ, | TM       |     |     |                 |     |     |     |          |      |     |     |  |

PRIORITY APPLN. INFO.:

IN 2004-CH885 A 20040902

AB The present invention relates to an improved process for the preparation of escitalopram which consists of a sequential double Grignard reaction on 5-iodophthalide to get the dihydroxy compound, its resolution using a chiral acid, cyclization of resolved compound, and cyanation of compound using DMF and CuCN. The present process utilizes the facile displacement of iodo group with cyano group in the final step of the preparation of escitalopram. Escitalopram is a widely used anti-depressant.

IT 878655-30-2P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; preparation of escitalopram)

RN 878655-30-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 128196-01-0P, Escitalopram 219861-08-2P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of escitalopram)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 219861-08-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 128196-01-0 CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:472143 CAPLUS

DOCUMENT NUMBER:

143:26491

TITLE:

A process for the preparation of high purity

escitalopram

CM 2

CRN 7601-90-3 CMF Cl H O4

IT 59729-33-8P, Citalopram 219861-08-2P, Escitalopram
 oxalate

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of high purity escitalopram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 219861-08-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (1:1) (9CI) (CA/INDEX NAME)

CM 1

CRN 128196-01-0 CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

RN 852705-14-7 CAPLUS

CN Methanesulfonic acid, trifluoro-, compd. with (1S)-5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-1-isobenzofuranpropanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 1493-13-6 CMF C H F3 O3 S

RN 852705-15-8 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 852705-13-6 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 75-75-2 CMF C H4 O3 S

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 852705-11-4 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, benzoate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 65-85-0 CMF C7 H6 O2

RN 852705-12-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 64169-39-7 CMF C19 H21 Br F N O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 852705-10-3 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, acetate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

Pullareddy, Muddasani; Sambasiva Rao, Talasila; INVENTOR(S):

PCT Int. Appl., 25 pp.

Srinivasa Rao, Nekkanti; Venkaiah Chowdary,

Nannapaneni

Natco Pharma Limited, India PATENT ASSIGNEE(S):

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

|                        | PATENT NO.    |     |     |             | KIND DATE          |      |               | APPLICATION NO. |                |                          |     |          | DATE     |     |     |     |     |     |    |
|------------------------|---------------|-----|-----|-------------|--------------------|------|---------------|-----------------|----------------|--------------------------|-----|----------|----------|-----|-----|-----|-----|-----|----|
|                        | WO 2005049596 |     |     | A1 20050602 |                    |      | WO 2003-IN363 |                 |                |                          |     | 20031120 |          |     |     |     |     |     |    |
|                        |               | W : | ΑE, | AG,         | AL,                | AM,  | ΑT,           | AU,             | ΑZ,            | BA,                      | BB, | BG,      | BR,      | BY, | ΒZ, | CA, | CH, | CN, |    |
|                        |               |     | CO, | CR,         | CU,                | CZ,  | DE,           | DK,             | DM,            | DZ,                      | EC, | EE,      | EG,      | ES, | FI, | GB, | GD, | GE, |    |
|                        |               |     | GH, | GM,         | HR,                | ΗU,  | ID,           | IL,             | IN,            | IS,                      | JP, | ΚE,      | KG,      | KΡ, | KR, | KZ, | LC, | LK, |    |
|                        |               |     | LR, | LS,         | LT,                | LU,  | LV,           | MA,             | MD,            | MG,                      | MK, | MN,      | MW,      | MX, | ΜZ, | NI, | NO, | NZ, |    |
|                        |               |     | OM, | PG,         | PH,                | PL,  | PT,           | RO,             | RU,            | SC,                      | SD, | SE,      | SG,      | SK, | SL, | SY, | ТJ, | TM, |    |
|                        |               |     | TN, | TR,         | TT,                | TZ,  | UA,           | UG,             | US,            | UZ,                      | VC, | VN,      | YU,      | ZA, | ZM, | ZW  |     |     |    |
|                        |               | RW: | BW, | GH,         | GM,                | KE,  | LS,           | MW,             | MZ,            | SD,                      | SL, | SZ,      | TZ,      | UG, | ZM, | ZW, | AM, | ΑZ, |    |
|                        |               |     | BY, | KG,         | KZ,                | MD,  | RU,           | ТJ,             | TM,            | ΑT,                      | BE, | BG,      | CH,      | CY, | CZ, | DE, | DK, | EE, |    |
|                        |               |     | ES, | FI,         | FR,                | GB,  | GR,           | HU,             | ΙE,            | IT,                      | LU, | MC,      | NL,      | PT, | RO, | SE, | SI, | SK, |    |
|                        |               |     | TR, | BF,         | ВJ,                | CF,  | CG,           | CI,             | CM,            | GΑ,                      | GN, | GQ,      | GW,      | ML, | MR, | NE, | SN, | TD, | TG |
| AU 2003282383          |               |     |     | A1          |                    | 2005 | 0608          | i               | AU 2003-282383 |                          |     |          | 20031120 |     |     |     |     |     |    |
| PRIORITY APPLN. INFO.: |               |     |     |             | WC                 |      |               |                 |                | WO 2003-IN363 A 20031120 |     |          |          |     |     |     |     |     |    |
| OTHER SOURCE(S):       |               |     |     | CASI        | CASREACT 143:26491 |      |               |                 |                |                          |     |          |          |     |     |     |     |     |    |
| GI                     |               |     |     |             |                    |      |               |                 |                |                          |     |          |          |     |     |     |     |     |    |

The present invention discloses an improved process for the preparation of high purity escitalopram base (I, R = CN) by reacting the acid addition salt of I (R = Br) with copper(I) cyanide and with or without copper(I) iodide in DMF medium at 145-150 °C. Cyanation of the acid addition salt is superior in yield and quality over the parent base compound I (R = Br). process is compatible to scale up operations thereby making the process com. viable for escitalopram oxalate. Escitalopram oxalate is an antidepressant available in the market.

64372-43-6P 128196-01-0P, Escitalopram 852705-10-3P 852705-11-4P 852705-12-5P 852705-13-6P 852705-14-7P 852705-15-8P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of high purity escitalopram) 64372-43-6 CAPLUS RN

Ι

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

IT 64169-39-7

RL: RCT (Reactant); REM (Removal or disposal); PROC (Process); RACT (Reactant or reagent)

(process for purification of citalopram by hydrogenolysis halogenated impurities)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:691476 CAPLUS

DOCUMENT NUMBER: 141:207048

TITLE: Preparation of pure citalogram

INVENTOR(S): Kaushik, Vipin Kumar; Rao, Divvela Venkata Naga

Srinivasa; Handa, Vijay Kumar; Sivakumaran,

Meenakshisunderam

PATENT ASSIGNEE(S): Aurobindo Pharma Ltd., India

SOURCE: U.S., 3 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
|                        |      |          |                 |          |
| US 6781003             | B1   | 20040824 | US 2003-456135  | 20030609 |
| PRIORITY APPLN. INFO.: |      |          | US 2003-456135  | 20030609 |

OTHER SOURCE(S): CASREACT 141:207048

GT

The present invention relates to an industrially advantageous method for the purification of citalopram (I) wherein desmethyl citalopram (II), present in crude citalopram as an impurity, is methylated to produce pure citalopram I. The resulting citalopram product I is isolated as the base or a pharmaceutically acceptable salt thereof. Thus, to crude citalopram (90 g, 0.28 mol) containing desmethyl citalopram (7 %, HPLC), formic acid (98%, 2.7 g) was added followed by aqueous formaldehyde(35%, 2.37 g). The reaction mass was heated at 85-95° for 30 min, cooled to 30°, and diluted with ethanol (900 mL), treated with oxalic acid dihydrate (41.94 g, 0.33 mol), and heated to reflux. The obtained solution was cooled to 20-25° and stirring was continued for 2 h at 20-25°, followed by collecting the product by filtration and recrystn. from ethanol to give highly pure 92 g crystalline citalopram oxalate having HPLC purity 99.7% wherein desmethyl citalopram (impurity) was not detected.

IT **59729-33-8P**, Citalopram

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(preparation of pure citalopram by N-methylation of crude citalopram containing

desmethyl citalogram with formaldehyde and formic acid)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

US 7019153

B2 20060328

PRIORITY APPLN. INFO.: OTHER SOURCE(S):

IN 2003-MU602

A 20030610

II

GT

MARPAT 142:56160

The present invention provides a process for decreasing the content of halogenated isobenzofuran impurities I (X = halo) in citalopram (II) by hydrogenolysis to I (X = H). Thus, 5 g crude citalopram base containing 4.84% of bromo impurity I (X = Br) is dissolved in 50 mL EtOAc, 0.1 g Pd/C and 0.1 g sodium hypophosphite added and the mixture refluxed for 2 h. Anal. showed that the bromo impurity I (X = Br) is absent.

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P,

Citalopram 207559-01-1P, Citalopram oxalate

RL: PUR (Purification or recovery); PREP (Preparation)
(process for purification of citalopram by hydrogenolysis halogenated impurities)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$O$$
 (CH<sub>2</sub>)<sub>3</sub>-NMe<sub>2</sub>

#### • HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RL: RCT (Reactant); RACT (Reactant or reagent)

(process for purification of citalopram via washing with polybasic acid solns.)

64169-39-7 CAPLUS RN

1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-CN dimethyl- (9CI) (CA INDEX NAME)

128196-01-0P, Escitalopram

RL: SPN (Synthetic preparation); PREP (Preparation)

(process for purification of citalopram via washing with polybasic acid solns.)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L45 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:1079731 CAPLUS

DOCUMENT NUMBER:

142:56160

TITLE:

process for purification of citalogram by

hydrogenolysis halogenated isobenzofuran impurities Borase, Ashok Punju; Patel, Nileshkumar Sureshbai;

Kilaru, Srinivasu; Thennati, Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceuticals Industries Ltd., India

SOURCE:

Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

INVENTOR(S):

FAMILY ACC. NUM. COUNT:

| PATENT NO.     | KIND DATE       | APPLICATION NO.         | DATE           |
|----------------|-----------------|-------------------------|----------------|
|                |                 |                         |                |
| EP 1486492     | A2 20041215     | EP 2004-291424          | 20040608       |
| EP 1486492     | A3 20050223     |                         |                |
| R: AT, BE, CH, | DE, DK, ES, FR, | GB, GR, IT, LI, LU, NL, | SE, MC, PT,    |
| IE, SI, LT,    | LV, FI, RO, MK, | CY, AL, TR, BG, CZ, EE, | HU, PL, SK, HR |
| US 2005004380  | A1 20050106     | US 2004-865139          | 20040608       |

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

1

ACCESSION NUMBER:

PATENT ASSIGNEE (S):

2005:120910 CAPLUS

DOCUMENT NUMBER:

142:197860

TITLE:

Process for purification of citalogram via washing

with polybasic acid solutions

INVENTOR (S):

Uttarwar, Sunil Govindrao; Gawli, Bhagwan Narayan

Meditab Specialities Pvt. Ltd., India; Wain,

Christopher Paul

SOURCE:

PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA      | PATENT NO.            |      |     |     | KIN        | D : | DATE |      | j   | APPL: | ICAT: | ION I | . 00   |     | D   | ATE  |     |
|---------|-----------------------|------|-----|-----|------------|-----|------|------|-----|-------|-------|-------|--------|-----|-----|------|-----|
| WO      | 2005                  | 0122 | 78  |     | A2         | _   | 2005 | 0210 | 1   | WO 2  | 004-0 | GB32  | <br>09 |     | 2   | 0040 | 723 |
| WO      | 2005                  | 0122 | 78  |     | <b>A</b> 3 |     | 2005 | 0616 |     |       |       |       |        |     |     |      |     |
|         | W :                   | ΑE,  | AG, | AL, | AM,        | AT, | AU,  | ΑZ,  | BA, | BB,   | BG,   | BR,   | BW,    | BY, | BZ, | CA,  | CH, |
|         |                       | CN,  | CO, | CR, | CU,        | CZ, | DE,  | DK,  | DM, | DZ,   | EC,   | EE,   | EG,    | ES, | FI, | GB,  | GD, |
|         |                       | GE,  | GH, | GM, | HR,        | HU, | ID,  | IL,  | IN, | IS,   | JP,   | KE,   | KG,    | ΚP, | KR, | KZ,  | LC, |
|         |                       | LK,  | LR, | LS, | LT,        | LU, | LV,  | MA,  | MD, | MG,   | MK,   | MN,   | MW,    | MX, | MZ, | NA,  | NI, |
|         | NO, NZ, O             |      |     |     |            | PH, | PL,  | PT,  | RO, | RU,   | SC,   | SD,   | SE,    | SG, | SK, | SL,  | SY, |
|         | TJ, TM, T             |      |     |     |            | TT, | TZ,  | UA,  | UG, | US,   | UZ,   | VC,   | VN,    | ΥU, | ZA, | ZM,  | ZW  |
|         | RW:                   | BW,  | GH, | GM, | KE,        | LS, | MW,  | MZ,  | NA, | SD,   | SL,   | SZ,   | TZ,    | UG, | ZM, | ZW,  | AM, |
|         |                       | AZ,  | BY, | KG, | KZ,        | MD, | RU,  | ТJ,  | TM, | AT,   | BE,   | BG,   | CH,    | CY, | CZ, | DE,  | DK, |
|         |                       | EE,  | ES, | FI, | FR,        | GB, | GR,  | HU,  | ΙE, | IT,   | LU,   | MC,   | NL,    | PL, | PT, | RO,  | SE, |
|         |                       | SI,  | SK, | TR, | BF,        | ВJ, | CF,  | CG,  | CI, | CM,   | GA,   | GN,   | GQ,    | GW, | ML, | MR,  | NE, |
|         |                       |      | TD, |     |            |     |      |      |     |       |       |       |        |     |     |      |     |
| GB      | GB 2418916            |      |     |     |            |     | 2006 | 0412 | +   | GB 2  | 006-  | 1023  |        |     | 2   | 0040 | 723 |
| PRIORIT | RIORITY APPLN. INFO.: |      |     |     |            |     |      |      |     | GB 2  | 003-  | 1747  | 5      | 1   | A 2 | 0030 | 725 |
|         |                       |      |     |     |            |     |      |      | 1   | WO 2  | 004-0 | GB32  | 09     | 1   | v 2 | 0040 | 723 |

OTHER SOURCE(S):

CASREACT 142:197860

AB A process for purification of racemic or optically active citalopram (I) comprises (i) providing crude I containing ≥1 I derivs. dissolved in a H2O-immiscible organic solvent, (ii) washing the crude mixture with ≥1 dilute aqueous solution of a polybasic acid, either in free form or as a partial

alkali metal salt, so as to sep. I from impurities present in the crude mixture; and (iii) where required converting purified I free base to a pharmaceutically acceptable salt. Thus, 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile was heated at 105° in aqueous H3PO4 followed by cooling, dilution with H2O, pH adjustment to 8-10 with aqueous NH3, and extraction with EtOAc. The EtOAc

layer

was washed with aqueous disodium edetate followed by drying over Na2SO4, treatment with decolorizing C, and filtration to give >99.85% pure citalopram hydrobromide.

IT **59729-33-8P**, Citalopram

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (process for purification of citalogram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

IT 59729-32-7P, Citalopram hydrobromide

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (process for purification of citalogram via washing with polybasic acid solns.)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$NC$$
 $O$ 
 $CH_2)_3-NMe_2$ 
 $F$ 

• HBr

IT 64169-39-7

A processes for preparation of escitalopram, useful as TITLE:

antidepressant

INVENTOR (S): Nannapaneni, Venkaiah Chowdary; Muddasani, Pulla

Reddy; Talasila, Sambashiva Rao; Nekkanti, Srinivasa

Rao; Podile, Khadgapathi

Natco Pharma Limited, India PATENT ASSIGNEE(S):

PCT Int. Appl., 30 pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA'     | PATENT NO.            |      |     |     |     | )    | DATE |      | 1   | APPL | ICAT: | I NO | . O <i>l</i> |     | D   | ATE  |     |
|---------|-----------------------|------|-----|-----|-----|------|------|------|-----|------|-------|------|--------------|-----|-----|------|-----|
|         |                       |      |     |     |     | -    |      |      |     |      |       |      |              |     | -   |      |     |
| WO      | 2004                  | 0653 | 75  |     | A1  | :    | 2004 | 0805 | 1   | WO 2 | 003-3 | [N22 | )            |     | 2   | 0030 | 617 |
|         | W:                    | ΑE,  | AG, | AL, | AM, | AT,  | AU,  | ΑZ,  | BA, | BB,  | BG,   | BR,  | BY,          | ΒZ, | CA, | CH,  | CN, |
| •       |                       | CO,  | CR, | CU, | CZ, | DE,  | DK,  | DM,  | DZ, | EC,  | EE,   | ES,  | FI,          | GB, | GD, | GE,  | GH, |
|         |                       | GM,  | HR, | ΗU, | ID, | IL,  | IN,  | IS,  | JP, | KE,  | KG,   | KP,  | KR,          | KZ, | LC, | LK,  | LR, |
|         | LS, LT, LU            |      |     |     | LV, | MA,  | MD,  | MG,  | MK, | MN,  | MW,   | MX,  | MZ,          | NI, | NO, | NZ,  | OM, |
|         | PH, PL, PI            |      |     | PT, | RO, | RU,  | SC,  | SD,  | SE, | SG,  | SK,   | SL,  | ТJ,          | TM, | TN, | TR,  | TT, |
|         | TZ, UA, UC            |      | UG, | US, | UZ, | VC,  | VN,  | YU,  | ZA, | ZM,  | zw    |      |              |     |     |      |     |
|         | RW:                   | GH,  | GM, | ΚE, | LS, | MW,  | MZ,  | SD,  | SL, | SZ,  | TZ,   | UG,  | ZM,          | ZW, | AM, | AZ,  | BY, |
|         |                       | KG,  | ΚZ, | MD, | RU, | TJ,  | TM,  | ΑT,  | BE, | BG,  | CH,   | CY,  | CZ,          | DE, | DK, | EE,  | ES, |
|         |                       | FI,  | FR, | GB, | GR, | HU,  | ΙE,  | IT,  | LU, | MC,  | NL,   | PT,  | RO,          | SE, | SI, | SK,  | TR, |
|         | BF, BJ, CF            |      |     | CF, | CG, | CI,  | CM,  | GA,  | GN, | GQ,  | GW,   | ML,  | MR,          | NE, | SN, | TD,  | TG  |
| AU      | AU 2003242990         |      |     |     | A1  |      | 2004 | 0813 | 1   | AU 2 | 003-2 | 2429 | 90.          |     | 2   | 0030 | 617 |
| PRIORIT | RIORITY APPLN. INFO.: |      |     | . : |     |      |      |      |     | IN 2 | 1-200 | 1A52 |              | Ž   | A 2 | 0030 | 117 |
|         |                       |      |     |     | 1   | WO 2 | 003- | IN22 | 0   | I    | W 2   | 0030 | 617          |     |     |      |     |

OTHER SOURCE(S):

CASREACT 141:157024

GΙ

The present invention relates to an improved process for the preparation of AB escitalopram (I) which consist of a sequential double Grignard reaction on 5-bromophthalide, isolation of di-magnesium salt, neutralization of di-magnesium salt, resolution of dihydroxy compound of the formula II, cyclization, and cyanation. The proposed process utilizes the insol. property of di-magnesium salt in a mixture of THF and a non-polar organic solvent, and separates it from impurities by simple filtration thereby making the isolation and purification process simple. Advantages of the proposed process include (a) high yield preparation of escitalopram (>25%), (b) escitalopram can be prepared in a simple and easy to adopt manner without involving any purification steps, (c) the process produces pure (>98%)

IT 59729-32-7P, Citalopram Hydrobromide

RL: IMF (Industrial manufacture); SPN (Synthetic

preparation); PREP (Preparation)

(preparation of pure citalopram by N-methylation of crude citalopram containing

desmethyl citalopram with formaldehyde and formic acid)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$O$$
 (CH<sub>2</sub>)<sub>3</sub>-NMe<sub>2</sub>

HBr

IT **64169-39-7**, 5-Bromo-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pure citalopram by N-methylation of crude citalopram containing desmethyl citalopram with formaldehyde and formic acid)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:633919 CAPLUS

DOCUMENT NUMBER: 141:157024

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:331827 CAPLUS

DOCUMENT NUMBER: 140:357194

Process for the manufacture of citalopram hydrobromide TITLE:

from 5-bromophthalide

INVENTOR(S): Chodankar, Nandkumar; Bhobe, Ajit; Oak, G. M.; Eappan,

Philip

Sekhsaria Chemicals Limited, India PATENT ASSIGNEE(S):

SOURCE:

U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
|                        |      |          |                 |          |
| US 2004077870          | A1   | 20040422 | US 2002-277451  | 20021022 |
| US 6812355             | B2   | 20041102 |                 |          |
| PRIORITY APPLN. INFO.: |      |          | US 2002-277451  | 20021022 |

CASREACT 140:357194; MARPAT 140:357194 OTHER SOURCE(S): Disclosed is a process for the preparation of 1-(4-fluorophenyl)-1-(3dimethylamino-propyl)-5-phthalanecarbonitrile (citalopram) (known antidepressant) or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide using p-fluorobromobenzene and then N,N-dimethylaminopropylmagnesium chloride, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and

improvinġ yields. 64169-39-7P, 1-(4-Fluorophenyl)-1-(3-dimethylaminopropyl)-5-IT bromophthalane

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic

preparation); PREP (Preparation); RACT (Reactant or reagent)
(manufacture of citalopram hydrobromide from 5-bromophthalide by two successive Grignard reactions on 5-bromophthalide using p-fluorobromobenzene and then N,N-dimethylaminopropylmagnesium

chloride)

64169-39-7 CAPLUS RN

1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-CN dimethyl- (9CI) (CA INDEX NAME)

59729-32-7P, Citalopram hydrobromide 59729-33-8P 207559-01-1P, Citalopram oxalate 500733-84-6P,

Citalopram acetate

RL: IMF (Industrial manufacture); SPN (Synthetic

preparation); PREP (Preparation)

(manufacture of citalopram hydrobromide from 5-bromophthalide by two successive Grignard reactions on 5-bromophthalide using

di-magnesium salt of intermediate compound was isolated, etc.

IT 128196-01-0P, Escitalopram 128196-02-1P,

R-(-)-Citalopram

 $\mathtt{RL}\colon \mathbf{IMF}$  (Industrial manufacture);  $\mathtt{SPN}$  (Synthetic

preparation); PREP (Preparation)

(processes for the preparation of escitalopram and its precursor)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-

fluorophenyl) -1,3-dihydro-, (1S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 128196-02-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 488148-14-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(processes for the preparation of escitalopram and its precursor)

RN 488148-14-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

p-fluorobromobenzene and then N,N-dimethylaminopropylmagnesium chloride)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$O$$
 (CH<sub>2</sub>)<sub>3</sub>-NMe<sub>2</sub>

### HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 500733-84-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 64-19-7 CMF C2 H4 O2

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:101152 CAPLUS

DOCUMENT NUMBER: TITLE:

140:145992

Process for the preparation of 1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile

INVENTOR(S): Hilden, Leif; Rumm

Hilden, Leif; Rummakko, Petteri; Grumann, Arne;

Pietikaeinen, Pekka

PATENT ASSIGNEE(S): Orion Corporation Fermion, Finland

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

7

| PATENT 1 | NO. |     |     | KIN  | D    | DATE |      |      | APPL | ICAT: | ION 1 | . O <i>l</i> |      | D   | ATE |     |
|----------|-----|-----|-----|------|------|------|------|------|------|-------|-------|--------------|------|-----|-----|-----|
|          |     |     |     |      | _    |      |      |      |      |       |       |              |      | _   |     |     |
| WO 2004  |     | A1  |     | 2004 | 0205 |      | WO 2 | 003- | FI55 | 7     |       | 2            | 0030 | 710 |     |     |
| W:       | ΑE, | AG, | AL, | AM,  | ΑT,  | AU,  | ΑZ,  | BA,  | BB,  | BG,   | BR,   | BY,          | ΒZ,  | CA, | CH, | CN, |
|          | CO, | CR, | CU, | CZ,  | DE,  | DK,  | DM,  | DZ,  | EC,  | EE,   | ES,   | FΙ,          | GB,  | GD, | GE, | GH, |
|          | GM, | HR, | HU, | ID,  | ΙL,  | IN,  | IS,  | JΡ,  | KE,  | KG,   | ΚP,   | KR,          | KΖ,  | LC, | LK, | LR, |

REFERENCE COUNT:

THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS 11 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:837069 CAPLUS

DOCUMENT NUMBER:

139:337880

TITLE:

Preparation of escitalopram via the chiral enriched diol monoesters of (4-bromo-2-(hydroxymethyl)phenyl)-

(4-fluorophenyl) methanol

INVENTOR(S):

Tse, Hoi Lun Allan

PATENT ASSIGNEE(S):

Torcan Chemical Ltd., Can.

SOURCE:

PCT Int. Appl., 30 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

| PATENT      | NO.                   |     | KINI | D   | DATE |       | 1    | APPL | ICAT:    | ION 1    | . 01 |        | D   | ATE |       |     |
|-------------|-----------------------|-----|------|-----|------|-------|------|------|----------|----------|------|--------|-----|-----|-------|-----|
| WO 200      | <br>30870             | 81  |      | A1  | -    | 2003  | 1023 | 1    | <br>WO 2 | <br>003- | CA52 | ·<br>2 |     | 2   | 00304 | 108 |
| W:          | ΑE,                   | AG, | AL,  | AM, | ΑT,  | AU,   | ΑZ,  | BA,  | BB,      | BG,      | BR,  | BY,    | ΒZ, | CA, | CH,   | CN, |
|             | CO,                   | CR, | CU,  | CZ, | DE,  | DK,   | DM,  | DZ,  | EC,      | EE,      | ES,  | FI,    | GB, | GD, | GE,   | GH, |
|             | GM,                   | HR, | HU,  | ID, | IL,  | IN,   | IS,  | JP,  | KE,      | KG,      | ΚP,  | KR,    | ΚZ, | LC, | LK,   | LR, |
|             | LS,                   | LT, | LU,  | LV, | MA,  | MD,   | MG,  | MK,  | MN,      | MW,      | MX,  | MZ,    | NI, | NO, | NZ,   | OM, |
|             | PH,                   | PL, | PT,  | RO, | RU,  | SC,   | SD,  | SE,  | SG,      | SK,      | SL,  | ТJ,    | TM, | TN, | TR,   | TT, |
|             | TZ,                   | UA, | UG,  | US, | UZ,  | VC,   | VN,  | YU,  | ZA,      | ZM,      | ZW   |        |     |     |       |     |
| RW          | : GH,                 | GM, | KE,  | LS, | MW,  | MZ,   | SD,  | SL,  | SZ,      | TZ,      | ŪĠ,  | ZM,    | ZW, | AM, | ΑZ,   | BY, |
|             | KG, KZ, MI            |     |      |     | ТJ,  | TM,   | AT,  | BE,  | ВG,      | CH,      | CY,  | CZ,    | DE, | DK, | EE,   | ES, |
|             | FI, FR, GI            |     |      |     |      | ΙE,   | IT,  | LU,  | MC,      | NL,      | PT,  | RO,    | SE, | SI, | SK,   | TR, |
|             | BF,                   | ВJ, | CF,  | CG, | CI,  | CM,   | GΑ,  | GN,  | GQ,      | GW,      | ML,  | MR,    | ΝE, | SN, | TD,   | TG  |
| CA 238      | 1341                  |     |      | AA  |      | 2003  | 1009 |      | CA 2     | 002-     | 2381 | 341    |     | 2   | 0020  | 409 |
| AU 200      | 32185                 | 75  |      | A1  |      | 2003  | 1027 |      | AU 2     | 003-     | 2185 | 75     |     | 2   | 0030  | 408 |
| EP 149      | 5013                  |     |      | A1  |      | 2005  | 0112 |      | EP 2     | 003-     | 7117 | 61     |     | 2   | 0030  | 408 |
| R:          | ΑT,                   | BE, | CH,  | DE, | DK,  | ES,   | FR,  | GB,  | GR,      | ΙT,      | LI,  | LU,    | NL, | SE, | MC,   | PT, |
|             | IE,                   | SI, | LT,  | LV, | FI,  | RO,   | MK,  | CY,  | AL,      | TR,      | BG,  | CZ,    | EE, | HU, | SK    |     |
| US 200      | US 2006009515         |     |      |     |      | 2006  | 0112 |      | US 2     | 005-     | 5108 | 90     |     | 2   | 0050  | 311 |
| PRIORITY AP | RIORITY APPLN. INFO.: |     |      |     |      |       |      |      | CA 2     | 002-     | 2381 | 341    |     | A 2 | 0020  | 409 |
|             |                       |     |      |     |      |       |      |      | WO 2     | 003-     | CA52 | 2      | 1   | W 2 | 0030  | 408 |
| OTHER SOURC | THER SOURCE(S):       |     |      |     |      | CT 13 | 9:33 | 7880 |          |          |      |        |     |     |       |     |

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003244676
                                20040216
                          Α1
                                            AU 2003-244676
                                                                    20030710
     US 2005209467
                                20050922
                          A1
                                            US 2005-45087
                                                                    20050131
PRIORITY APPLN. INFO.:
                                             FI 2002-1421
                                                                    20020730
                                            US 2002-419150P
                                                                 P
                                                                    20021018
                                             WO 2003-FI557
                                                                 W
                                                                    20030710
OTHER SOURCE(S):
                         CASREACT 140:145992; MARPAT 140:145992
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GI

AΒ The present invention is directed to novel processes for the preparation of citalopram comprising halogenation of a phthalides I (wherein R is a suitable group to be changed to CN) to afford an acid halides II (X is halogen) and thereafter obtaining citalogram through two successive reactions with suitable organometallic halides or organoboranes or by a reaction with organometallic 4-fluorophenylhalide or 4-fluorophenylborane followed by reduction and alkylation, and an exchange of R to cyano to afford citalopram. The order of the reactions can be varied depending e.g. on the starting compound used.

59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of citalopram)

RN59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-45-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of citalogram)

RN64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 219861-08-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 128196-01-0 CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:590880 CAPLUS

DOCUMENT NUMBER:

139:133459

TITLE:

Cyanation process for the preparation of citalogram

and its extractive purification

INVENTOR(S):

Coppi, Laura; Gasanz Guillen, Yolanda; Campon Pardo,

Julio

PATENT ASSIGNEE(S):

Esteve Quimica, S.A., Spain

SOURCE:

U.S. Pat. Appl. Publ., 5 pp.

$$\begin{array}{c} \text{Br} & \text{CH}_2-\text{O}-\text{COCH}_3 \\ \text{OH} & \text{OH} \\ \text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NMe}_2 \\ \text{F} & \text{II} \end{array}$$

AB Preparation of escitalopram (I) via the chiral enriched monoacetate ester of (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol (II) was disclosed. For example, a racemic mixture of monoacetate ester II (13.52 g) and (+)-di-p-toluoyl tartaric acid (11.92 g) in acetone (135 mL) was heated at reflux until a pale brown solution was obtained. The solution was cooled, the acetone removed under vacuum and the resulting brown foam recrystd. from acetone-hexane (2:1) to afford the (+)-di-p-toluoyl tartaric acid salt of monoacetate ester II with a diastereomeric ratio of 97:3. Of note, the claimed (+)-di-p-toluoyl tartaric acid salt of monoacetate ester II was converted to escitalopram oxalate in 4-steps with [α]D = +10.1° (at 20°C, c 0.95 in MeOH).

IT 488148-14-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of escitalopram via a chiral enriched diol monoester intermediate)

RN 488148-14-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)~ (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IT 128196-01-0P, Escitalopram 219861-08-2P, Escitalopram oxalate

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation)

; USES (Uses)
 (target compound; preparation of escitalopram via a chiral enriched diol
 monoester intermediate)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

|       | PATENT NO.                  |      |     |      |     |           | DATE |      |      | APPI | LICAT  | ION :      | NO.  | •   | D     | ATE  |      |         |
|-------|-----------------------------|------|-----|------|-----|-----------|------|------|------|------|--------|------------|------|-----|-------|------|------|---------|
|       | US                          | 2003 |     |      |     |           |      | 2003 | 0731 |      | US 2   | 2003-      | 3512 | 89  |       | 2    | 0030 | <br>124 |
|       | US                          | 6635 | 773 |      |     | B2        |      | 2003 | 1021 |      |        |            |      |     |       |      |      |         |
|       | ES                          | 2194 | 597 |      |     | <b>A1</b> |      | 2003 | 1116 |      | ES 2   | 2002-      | 167  |     |       | 2    | 0020 | 125     |
|       | ES                          | 2194 | 597 |      |     | B2        |      | 2004 | 0801 |      |        |            |      |     |       |      |      |         |
|       | CA                          | 2474 | 323 |      |     | AA        |      | 2003 | 0731 |      | CA 2   | 2003-:     | 2474 | 323 |       | 2    | 0030 | 124     |
|       |                             |      |     |      |     |           |      |      |      |      |        | 2003-      |      |     |       |      | 0030 |         |
|       |                             | W:   |     |      |     |           |      |      |      |      |        | , BG,      |      |     |       |      | CH,  | CN,     |
|       |                             |      |     |      |     |           |      |      |      |      |        | , EE,      |      |     |       |      |      |         |
|       |                             |      |     |      |     |           |      |      |      |      |        | , KG,      |      |     |       |      |      |         |
|       | LS, LT, LU<br>PL, PT, RO    |      |     |      |     |           |      |      |      |      |        |            |      |     |       |      |      |         |
|       |                             |      |     |      |     |           |      |      |      |      |        |            |      |     |       |      |      |         |
|       |                             |      |     |      |     |           |      | VN,  |      |      |        |            |      |     | •     | •    | •    | •       |
|       |                             | RW:  |     |      |     |           |      |      |      |      |        | , TZ,      | ŪĠ,  | ZM, | ZW,   | AM,  | AZ,  | BY,     |
|       |                             |      | KG, | ΚZ,  | MD, | RU,       | TJ,  | TM,  | AT,  | BE,  | BG,    | , CH,      | CY,  | CZ, | DE,   | DK,  | EE,  | ES,     |
|       |                             |      |     |      |     |           |      |      |      |      |        | , NL,      |      |     |       |      |      |         |
|       |                             |      |     |      |     |           |      |      |      |      |        | , ML,      |      |     |       |      |      | •       |
|       | ΕP                          | 1479 |     |      |     |           |      |      |      |      |        | 2003-      |      |     |       |      |      | 124     |
|       |                             | R:   | AT, | BE,  | CH, | DE,       | DK,  | ES,  | FR,  | GB,  | GR,    | , IT,      | LI,  | LU, | NL,   | SE,  | MC,  | PT,     |
|       |                             |      |     |      |     |           |      |      |      |      |        | TR,        |      |     |       |      |      |         |
|       | JP                          | 2005 |     |      |     |           |      |      |      |      |        |            |      |     |       |      | 0030 | 124     |
|       | JP 2005522419<br>CN 1688565 |      |     |      |     |           |      |      |      |      |        |            |      |     | 0030  | 124  |      |         |
|       | ZA 2004005441               |      |     |      |     |           |      |      |      |      |        |            |      |     | 0040  | 708  |      |         |
|       | NO 2004003568               |      |     |      |     |           |      |      |      |      |        |            |      |     | 00408 | 325  |      |         |
| PRIOF | ZTIS                        | APP  | LN. | INFO | . : |           |      |      |      |      | ES 2   | 2002-3     | 167  |     | 7     | A 20 | 0020 | 125     |
|       |                             |      |     |      |     |           |      |      | •    | WO 2 | 2003-1 | ES37       |      | ī   | v 20  | 0030 | 124  |         |
| רא    | <b>A</b>                    |      |     |      |     |           |      |      |      |      |        | <b>-</b> . |      |     |       | -    |      |         |

AB Crude citalopram was prepared the cyanation of 1-[3-(dimethylamine)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-bromoisobenzofuran with copper cyanide and purified citalopram or one of its salts (e.g., citalopram hydrobromide) was obtained by the extractive purification of citalopram by selective extns. of citalopram or it salts of its impurities with organic solvents (e.g., toluene and heptane) and water under specific conditions of pH and temperature TT 59729-33-8P, Citalopram

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cyanation process for the preparation of citalopram and its extractive purification)  $\label{eq:cyanation}$ 

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(cyanation process for the preparation of citalogram and its extractive purification)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

Br Me<sub>2</sub>N- (CH<sub>2</sub>)<sub>3</sub>

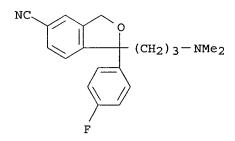
IT 59729-32-7P, Citalopram hydrobromide

RL: SPN (Synthetic preparation); PREP (Preparation)

(cyanation process for the preparation of citalogram and its extractive purification)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)



• HBr

L45 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:551309 CAPLUS

DOCUMENT NUMBER:

139:117333

TITLE:

Process for the preparation of 1-[3-

(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-

5-isobenzofurancarbonitrile via cyanation of the

corresponding chloride or bromide precursors.

INVENTOR(S):

Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai,

Rajendran; Patel, Nileshkumar Sureshbhai

PATENT ASSIGNEE(S): SOURCE:

Sun Pharmaceutical Industries Limited, India

JRCE: PCT Int. Appl., 41 pp. CODEN: PIXXD2

DOCUMENT TYPE: Pate

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2003-IN6
                                                                   20030107
    WO 2003057132
                          A2
                                20030717
    WO 2003057132
                          Α3
                                20040226
    WO 2003057132
                          Cl
                                20040415
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                20030724
                                           AU 2003-222435
    AU 2003222435
                          A1
                                            US 2004-500532
    US 2005043550
                          A1
                                20050224
                                                                   20040719 <--
PRIORITY APPLN. INFO.:
                                            IN 2002-MU10
                                                                A 20020107
                                            IN 2002-MU18
                                                                Α
                                                                   20020110
                                            IN 2002-MU847
                                                                Α
                                                                   20020930
                                            WO 2003-IN6
                                                                   20030107
                         CASREACT 139:117333; MARPAT 139:117333
OTHER SOURCE(S):
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GT

Title compound (I; R = cyano) (citalogram) was prepared by treatment of I (R = cyano) AΒ Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. PhMe layer was separated and the pH of the aqueous layer was adjusted to 9.0-9.5

with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and

0.23% of the amide and desmethylcitalopram resp.

59729-32-7P, Citalopram hydrobromide 59729-33-8P,

Ι

1-[3-(Dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5isobenzofurancarbonitrile

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of citalogram via cyanation of the corresponding chloride or bromide precursor)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$NC$$
  $O$   $(CH2)3-NMe2$ 

HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of citalogram via cyanation of the corresponding chloride or bromide precursor)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:282554 CAPLUS

DOCUMENT NUMBER:

138:305791

TITLE:

Process for the preparation of citalogram, and

intermediates and derivatives

INVENTOR(S):

Malik, A. Aslam; Palandoken, Hasan; Stringer, Joy A.; Huang, Dershing; Romero, Antonio; Dapremont, Olivier

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

L45 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:31487 CAPLUS

DOCUMENT NUMBER: 134:102526

TITLE: Process for the synthesis of citalogram

INVENTOR(S): Bolzonella, Eva; Castellin, Andrea; Nicole, Andrea

PATENT ASSIGNEE(S): Vis Farmaceutici S.p.A., Italy

SOURCE: PCT Int. Appl., 21 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Facence English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

AB

PATENT NO. KIND DATE APPLICATION NO. DATE \_\_\_\_\_ \_\_\_\_\_\_ \_\_\_\_\_\_ \_ \_ \_ \_ WO 2000-EP6426 20010111 20000706 WO 2001002383 A2 20010503 WO 2001002383 Α3 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG IT 1999-MI1486 IT 99MI1486 Α1 20010108 19990706 CA 2001-2383963 CA 2383963 20010706 AΑ 20020117 WO 2001-DK481 20020117 20010706 WO 2002004435 **A1** W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG BR 2001-6976 BR 2001006976 Α 20020723 20010706 NO 2002001118 Α 20020424 NO 2002-1118 20020306 US 2002-96149 US 2002128497 Α1 20020912 20020306 A 19990706 PRIORITY APPLN. INFO.: IT 1999-MI1486 A 20000706 W 20010706 WO 2000-EP6426 WO 2001-DK481

by the conversion of 1-(4'-fluorophenyl)1-3-(dimethylaminopropyl)-5-

A new process is described for the synthesis of citalopram characterized

AB A method for the preparation of citalopram is presented, comprising the reaction of isobenzofuranpropanamine I, wherein R is Cl or Br, with a cyanide source in the presence of a nickel catalyst and isolation of the corresponding 5-cyano compound, i.e. citalopram.

I

IT 64169-39-7, 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)1,3-dihydro-N,N-dimethyl- 64169-45-5, 1Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl-

RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the preparation of citalogram by nickel-catalyzed cyanation of halo precursors)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN

IT 59729-33-8P, Citalopram

RL: SPN (Synthetic preparation); PREP (Preparation) (method for the preparation of citalogram by nickel-catalyzed cyanation of halo precursors)
59729-33-8 CAPLUS

Saloni Sharma 06/19/2006

CH 2001-545

A 20010322

OTHER SOURCE(S):

CASREACT 135:61224; MARPAT 135:61224

 ${\tt AB} \quad {\tt A} \ {\tt process} \ {\tt for} \ {\tt the} \ {\tt preparation} \ {\tt and} \ {\tt purification} \ {\tt of} \ {\tt citalopram} \ ({\tt I}) \ {\tt is} \ {\tt presented} \ {\tt in}$ 

which a benzoisofuran derivative [II; Z = iodo, bromo, chloro, CF3(CF2)nS020; n = 0-8] is subjected to a cyanide-exchange reaction with a cyanide source (e.g., cuprous cyanide). The resultant crude citalopram is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent (e.g., acetic anhydride), the reaction mixture is then subjected to an acid/base wash and/or crystallization

and

recrystn. of citalopram in order to remove the amides formed from the crude citalopram mixture, and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt.

IT 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

Ι

(method for the preparation and purification of citalogram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7 64169-45-5 260066-78-2 RL: RCT (Reactant); RACT (Reactant or reagent) (method for the preparation of citalogram by the cyanidation of)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 260066-78-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:386023 CAPLUS

DOCUMENT NUMBER:

134:353251

TITLE:

Method for the preparation of citalogram by

nickel-catalyzed cyanation of halo precursors

INVENTOR(S):

Petersen, Hans; Rock, Michael Harold

PATENT ASSIGNEE(S):

H Lundbeck A/S, Den.

SOURCE:

Brit. UK Pat. Appl., 16 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

| PATENT NO.             | KIND   | DATE       | APPLICATION NO. | DATE           |
|------------------------|--------|------------|-----------------|----------------|
|                        |        |            |                 | - <del>-</del> |
| GB 2354240 A1          |        | 20010321   | GB 2001-1508    | 19991119       |
| PRIORITY APPLN. INFO.: |        |            | DK 1999-921 ·   | 19990625       |
|                        |        |            | WO 1999-DK643   | 19991119       |
| OTHER SOURCE(S):       | MARPAT | 134:353251 |                 |                |

RN 260066-78-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)

IT 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

L45 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:472398 CAPLUS

DOCUMENT NUMBER: 135:61224

TITLE: Method for the preparation and purification of

citalopram

INVENTOR(S): Villa, Marcos; Sbrogio, Federico; Dancer, Robert

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den. SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

| PATENT NO.     | KIND DATE   | E APPL        | ICATION NO.     | DATE        |
|----------------|-------------|---------------|-----------------|-------------|
|                |             |               |                 |             |
| WO 2001045483  | A2 2001     | 10628 WO 2    | 001-DK147       | 20010307    |
| WO 2001045483  | A3 2001     | 11227         |                 |             |
| W: AE, AG, AL, | AM, AT, AU, | , AZ, BA, BB, | BG, BR, BY, BZ, | CA, CH, CN, |
| CO, CR, CU,    | CZ, DE, DK, | , DM, DZ, EE, | ES, FI, GB, GD, | GE, GH, GM, |
| מז ווא או      | TI. TNI TS  | TD KE KG      | KP KP KZ LC     | T.K T.P T.S |

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LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
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        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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    EP 1462447
                        A3
                               20041117
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20040710 IN 2001-MA214
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A 20001222
A3 20010307
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PRIORITY APPLN. INFO.:
                                           NL 2001-1017525
                                           EP 2001-913726
                                           WO 2001-DK147
                                                               W 20010307
                                           GB 2001-5983
                                                              A3 20010312
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Saloni Sharma 06/19/2006

| EP 1181272              | В1  | 20020828                      |                         |            |            |
|-------------------------|-----|-------------------------------|-------------------------|------------|------------|
|                         |     |                               | GB, GR, IT, LI, LU, NL, | SE         | E. MC. PT. |
| IE, SI, LT,             |     |                               | ,,,,,                   |            | -,,        |
| BR 2001006271           | Α   | 20020521                      | BR 2001-6271            |            | 20010307   |
| TR 200200018            | T1  |                               |                         |            | 20010307   |
| AT 222899               | E   | 20020021                      |                         |            | 20010307   |
| PT 1181272              | T   | 20020313                      |                         |            | 20010307   |
| ES 2181663              | T3  |                               |                         |            | 20010307   |
|                         | T2  |                               |                         |            |            |
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| NL 1017534              | C1  |                               |                         |            | 20010308   |
| DK 200100386            | A5  |                               |                         |            | 20010308   |
| IN 193426               | A   |                               |                         |            | 20010309   |
| GB 2356199              | A1  |                               | GB 2001-5981            |            | 20010312   |
| GB 2356199              | B2  |                               |                         |            |            |
| CZ 293140               | В6  |                               |                         |            | 20010312   |
| FI 108640               | В1  |                               |                         |            | 20010313   |
| NO 2001001272           | Α   | 20020701                      |                         |            | 20010313   |
| NO 313047               | В1  |                               |                         |            |            |
| GR 2001100131           | Α   | 20021009                      |                         |            | 20010316   |
| DE 10112828             | C1  |                               | _                       |            | 20010316   |
| DE 10164725             | A1  | 20030206                      | DE 2001-10164725        |            | 20010316   |
| DE 10164725             | B4  |                               |                         |            |            |
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| BE 1013417              | A6  | 20011204                      | BE 2001-189             |            | 20010322   |
| FR 2818977              | A1  | 20020705                      | FR 2001-4025 .          |            | 20010326   |
| FR 2818977              | В1  | 20031205                      |                         |            |            |
| NL 1018410              | C1  | 20011113                      | NL 2001-1018410         |            | 20010628   |
| BE 1013316              | A6  | 20011106                      | BE 2001-466             |            | 20010709   |
| GB 2361697              | A1  | 20011031                      | GB 2001-17095           |            | 20010713   |
| IN 193611               | Α   | 20040724                      | IN 2001-MA580           |            | 20010713   |
| CH 691999               | Α   | 20010726                      | CH 2001-1412            |            | 20010726   |
| ES 2170733              | A1  | 20020801                      | ES 2001-1763            |            | 20010727   |
| ES 2170733              | В1  |                               |                         |            |            |
| AU 750006               | B1  |                               |                         |            | 20010827   |
| SE 2001003044           | Α   | 20020629                      |                         |            | 20010914   |
| ZA 2001010133           | Α   | 20030113                      |                         |            | 20011210   |
| BG 106219               | A   | 20020830                      |                         |            | 20011213   |
| US 2002087012           | A1  |                               |                         |            | 20011220   |
| US 6855834              | B2  |                               |                         |            |            |
| NZ 516299               | A   | 20021220                      |                         |            | 20011220   |
| HR 2002000005           | A1  | 20030430                      |                         |            | 20020104   |
| US 2003178295           | A1  |                               |                         |            | 20020104   |
| PRIORITY APPLN. INFO.:  | AT. | 20030723                      | DK 2000-1943            | Α          | 20030210   |
| THEORETT PRESENT AND ON |     |                               | WO 2001-DK148           | W          | 20010307   |
|                         |     |                               | NL 2001-DK148           | A          | 20010307   |
|                         |     |                               | CH 2001-101/334         | A          | 20010308   |
|                         |     |                               | US 2001-35005           |            | 20010322   |
| OTHER SOURCE(S):        | CAC | <b>₽</b> ₽ልሮፕ 135. <i>6</i> 1 | 225; MARPAT 135:61225   | <b>~</b> 1 | 20011220   |
| GI                      | CAS | MACI 133.01                   | 225, PRACE TO 101220    |            |            |

Saloni Sharma 06/19/2006

AB High-purity citalopram (I) is prepared on an industrial scale by: subjecting a citalopram precursor [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] (e.g., Z = Br) to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source (e.g., CuCN) in a solvent (e.g., sulfolane); the crude citalopram product is optionally subjected to some initial purification and the crude citalopram base is subsequently subjected to a thin- or falling-film distillation process.

IT 64169-39-7 64169-45-5 260066-78-2

RL: RCT (Reactant); RACT (Reactant or reagent)

II

(in a process for the preparation of high-purity citalogram by cyanidation with purification via thin-film distillation)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

Saloni Sharma

#### (CA INDEX NAME) dimethyl- (9CI)

64169-45-5 CAPLUS RN

1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-CNdimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:489362 CAPLUS

DOCUMENT NUMBER:

135:61225

TITLE:

Process for the preparation of high-purity citalogram

by cyanidation with purification via thin-film

distillation

INVENTOR(S):

Castellin, Andrea; Volpe, Giulio; Sbrogio, Federico

PATENT ASSIGNEE(S):

SOURCE:

H. Lundbeck A/s, Den. PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

| PATENT NO. |      |      |     |                            | KIN            | )   | DATE |      |     | APPL: | ICAT | ION 1 | <b>10</b> . |     | D   | ATE   |     |
|------------|------|------|-----|----------------------------|----------------|-----|------|------|-----|-------|------|-------|-------------|-----|-----|-------|-----|
|            |      |      |     |                            |                | -   |      |      |     |       |      |       |             |     |     |       |     |
| WO         | 2001 | 0478 | 77  |                            | A2             |     | 2001 | 0705 | 1   | WO 2  | 001- | DK14  | 8           |     | 20  | 0010  | 307 |
| WO         | 2001 | 0478 | 77  |                            | А3             |     | 2000 | 1227 |     |       |      |       |             |     |     |       |     |
|            | W:   | ΑE,  | AG, | AL,                        | AM,            | AT, | AU,  | AZ,  | BA, | BB,   | BG,  | BR,   | BY,         | BZ, | CA, | CH,   | CN, |
|            |      |      |     |                            |                |     | DK,  |      |     |       |      |       |             |     |     |       |     |
|            |      | •    | •   | •                          | •              | •   | IS,  | •    | •   | •     | •    | •     | •           | •   | •   | •     | •   |
|            |      |      | -   |                            |                |     | MG,  |      |     |       | •    | •     |             | •   | •   |       |     |
|            |      |      |     |                            | SG, SI, SK, SI |     |      | -    |     |       |      | -     |             |     |     |       |     |
|            |      | •    | -   | -                          | ZW             |     |      |      | 10, | 111,  | 110, | 11,   | 14,         | UA, | 00, | 05,   | 04, |
|            | D1.1 | •    | •   | •                          |                |     |      | an.  |     | 0.5   |      |       |             |     | - · | CII   | ~~. |
|            | RW:  | GH,  | GM, | KE,                        | LS,            | MW, | MZ,  | SD,  | SL, | SZ,   | 12,  | UG,   | ZW,         | ΑT, | BE, | CH,   | CY, |
|            |      | DE,  | DK, | ES,                        | FI,            | FR, | GB,  | GR,  | ΙĖ, | IT,   | LU,  | MC,   | NL,         | PT, | SE, | TR,   | BF, |
|            |      | ВJ,  | CF, | CG,                        | CI,            | CM, | GA,  | GN,  | GW, | ML,   | MR,  | ΝE,   | SN,         | TD, | TG  |       |     |
| CA         | 2359 | 810  |     |                            | AA             |     | 2001 | 0705 |     | CA 2  | 001- | 2359  | 810         |     | 20  | 0010  | 307 |
| CA         | 2359 | 810  |     |                            | С              |     | 2002 | 1105 |     |       |      |       |             |     |     |       |     |
| ΑIJ        | 2001 | 0392 |     |                            | C 20<br>A5 20  |     |      |      |     | AU 2  | 001- | 3920  | 2           |     | 20  | 0010  | 307 |
|            | 2001 |      |     |                            |                |     |      |      |     |       |      |       |             |     |     | 0010  |     |
|            | 2001 | •    |     | A4 20011101<br>B4 20020321 |                |     |      |      | •   | Z     | 001  | 1005  | ,,          |     | 2   | 0010. | 507 |
|            |      |      | פפ  |                            |                |     |      |      |     | - A   | 001  | 0100  |             |     | ~   | 2010  | 200 |
| EΡ         | 1181 | 272  |     |                            |                |     |      |      |     | EP 2  | 001- | 9137  | 27          |     | 20  | 0010  | 307 |

L45 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:592319 CAPLUS

Correction of: 2001:386023

DOCUMENT NUMBER:

135:137393

Correction of: 134:353251

TITLE: INVENTOR(S): Method for the preparation of citalogram Petersen, Hans; Rock, Michael Harold

PATENT ASSIGNEE(S):

H Lundbeck A/S, Den.

SOURCE:

Brit. UK Pat. Appl., 15 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 1

|          |     | CENT NO.                             |             |          |   |            |   |      |       |     |      | LICAT                            |               | NO.        |     | D      | ATE          |     |
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|          | GB  | 2354:                                | 240         |          |   | A1         | - |      |       |     |      | 200 <u>1</u> -<br>1999-<br>1999- |               |            |     | 1:     | 9991         | 119 |
|          | GB  | 2354                                 | 240         |          |   | B2         |   | 2001 | 0523  |     |      | )                                |               |            |     |        |              |     |
| <b>)</b> | IT  | 99MI                                 | 1579        |          |   | <b>A</b> 1 |   | 2001 | 0115  |     | IT   | 1999-                            | MI15          | 79         |     | 1      | 9990         | 715 |
|          | WO  | 2000                                 | 0119        | 26       |   | A2         |   | 2000 | 0309  | ,   | WO   | 1999-                            | DK64          | 3          |     | 1:     | 9991         | 119 |
|          | WO  | 2000                                 | 0119        | 26       |   | A3         |   | 2000 | 062,9 |     |      |                                  |               |            |     |        |              |     |
|          |     | W:                                   | •           |          |   | -          |   | -    | -     |     |      | , BR,                            |               |            |     |        |              |     |
|          |     |                                      |             |          | • | •          |   | •    |       |     |      | , GM,                            |               | -          |     |        |              |     |
|          |     |                                      |             |          |   |            |   |      |       |     |      | , LS,                            |               |            |     |        |              |     |
|          |     |                                      |             | •        | • |            |   | •    | •     | •   |      | , SD,                            | •             | SG,        | SI, | SK,    | SL,          | ТJ, |
|          |     |                                      | •           |          |   |            |   |      | •     | •   |      | , ZA,                            |               |            |     |        |              |     |
|          |     | RW:                                  |             |          |   |            |   |      |       |     |      | , UG,                            |               |            |     |        |              |     |
|          |     |                                      | -           |          | - |            |   | •    | -     | -   |      | , DK,                            | -             | -          |     | -      | •            |     |
|          |     |                                      |             |          |   |            |   | SE,  | BF,   | ΒJ, | CF   | , CG,                            | CI,           | CM,        | GA, | GN,    | GW,          | ML, |
|          |     |                                      |             | NΕ,      |   |            |   |      |       |     |      |                                  |               |            |     |        |              |     |
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|          | EΡ  | 1105                                 |             |          |   |            |   |      | 0213  |     |      |                                  |               |            |     |        |              |     |
|          |     | R:                                   |             | •        |   | •          | • | •    | FR,   | GB, | GR   | , IT,                            | LI,           | LU,        | NL, | SE,    | MC,          | PT, |
|          |     |                                      |             | SI,      |   |            |   |      |       |     |      |                                  |               |            |     |        |              |     |
|          |     | 1998                                 |             |          |   | T          |   |      |       |     | DE   | 1999-                            | 1998          | 3486       |     | 1      | 9991         | 119 |
|          |     | 1998                                 |             |          |   |            |   |      | 0905  |     | 3.77 | 0001                             | 0001          | 1001       | 2 2 |        | 0001         |     |
|          | AU  | 2001                                 | 1004        | 33       |   | A4         |   |      | 1101  |     | ΑU   | 2001-                            | -2001         | 1004       | 33  | T      |              | 119 |
|          | AU  | 2001                                 | 1004        | 33       |   | B4         |   |      | 0117  |     | 3 m  | 1999-                            | 0.000         | 0.0        |     | -      |              | 110 |
|          | AT  | 2132                                 | 3/          |          |   | 프          |   | 2002 | 0215  |     | ΗI   | 1999-                            | 1726          | 7          |     |        |              |     |
|          | אמ  | 2001<br>2001<br>2132<br>9917<br>9909 | 30 /<br>040 |          |   | A.         |   | 2002 | 0515  |     | אם   | 1999-                            | . 1 / 2 0     | ,          |     |        | 9991<br>9991 |     |
|          | ΑT  | 4099                                 | 040<br>60   |          |   | A<br>D     |   |      | 1227  |     | ΑI   | 1333-                            | -9040         |            |     | 1      | フフフエ         | 117 |
|          |     | 2001                                 | 00          | 0        |   | m o        |   |      | 0521  |     | מנים | 2001-                            | 2001          | 0270       | ^   | -      | 0001         | 110 |
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|          |     | 3389                                 |             | <b>3</b> |   |            |   | _    | 0730  |     | UP   | 2000                             | -3670         | 65         |     | 1      | フフフエ         | 117 |
|          |     | 1105                                 |             | •        |   | ΒZ<br>T    |   |      | 0731  |     | חת   | 1999-                            | 0600          | 06         |     | 1      | 0001         | 110 |
|          |     | 2172                                 |             |          |   | T3         |   |      |       |     |      | 1999                             |               |            |     |        |              |     |
|          |     |                                      | 330<br>74   |          |   | 13         |   | 2002 | 0710  |     | C 7  | 2001                             | - J00∠<br>210 | Ub         |     | 1      | 9991<br>9991 | 110 |
|          | -   | 1129                                 | 174<br>9593 |          |   | D D        |   | 2003 | 1202  |     | CM   | 1999                             | 01 <i>67</i>  | <i>c</i> 0 |     | 1<br>T | <b>2221</b>  | 110 |
|          | CIN | 1129                                 | <b>5</b> 73 |          |   | В          |   | ∠003 | 1203  |     | CIA  | T 3 3 3 .                        | -910\         | 00         |     | 1      | フフフエ         | 117 |

| NZ 514982              | Α  | 20040130 | NZ | 1999-514982  |     | 19991119 |
|------------------------|----|----------|----|--------------|-----|----------|
| CA 2290125             | AA | 20001225 | CA | 1999-2290125 |     | 19991122 |
| CA 2290125             | С  | 20040810 |    |              |     |          |
| NO 2001000318          | A  | 20010220 | NO | 2001-318     |     | 20010119 |
| SE 2001000194          | Α  | 20010425 | SE | 2001-194     |     | 20010124 |
| SE 516689              | C2 | 20020212 |    |              |     |          |
| FI 2001000154          | A  | 20010209 | FI | 2001-154     |     | 20010125 |
| FI 108538              | B1 | 20020215 |    |              |     |          |
| ZA 2001007956          | Α  | 20020927 | ZA | 2001-7956    |     | 20010927 |
| ZA 2001008855          | A  | 20020611 | ZA | 2001-8855    |     | 20011026 |
| US 2002061925          | A1 | 20020523 | US | 2001-12025   |     | 20011106 |
| US 6750358             | B2 | 20040615 |    |              |     |          |
| BG 106190              | Α  | 20020830 | BG | 2001-106190  |     | 20011207 |
| ZA 2002005023          | A  | 20030623 | ZA | 2002-5023    |     | 20020621 |
| HK 1047745             | A1 | 20040910 | HK | 2002-109330  |     | 20021224 |
| PRIORITY APPLN. INFO.: |    |          | DK | 1999-921     | . А | 19990625 |
|                        |    |          | WO | 1999-DK643   | W   | 19991119 |

OTHER SOURCE(S):

GI

CASREACT 135:137393; MARPAT 135:137393

AB A method for preparing the antidepressant, citalopram [I; R = CN], by reacting an isobenzofuranpropanamine [I; R = Cl or Br] with a cyanide source in the presence of a nickel catalyst is presented. Citalopram is produced in high yield as a very pure product using this catalytic process. Thus, sequential addition of I (R = Cl) and NaCN to the Ni catalyst formed by reflux of NiCl2 with PPh3 in AcCN in the presence of a catalytic amount of Zn, followed by workup and treatment with oxalic acid, gave citalopram oxalate in 55% yield.

IT 59729-33-8P 128196-01-0P, (S)-Citalopram

207559-01-1P, Citalopram oxalate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

Ι

(preparation of citalogram by nickel-catalyzed cyanation of halo precursors)

RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

| GB 2365865<br>US 2002025982               | B2<br>A1       | 20020717<br>20020228             | US 2001-930107                       | 20010814                    |
|---|----------------|----------------------------------|--------------------------------------|-----------------------------|
| US 6426422<br>US 2002026062<br>US 6509483 | B2<br>A1<br>B2 | 20020730<br>20020228<br>20030121 | US 2001-930110                       | 20010814                    |
| WO 2002016341                             | A1             | 20020228                         | WO 2001-DK541<br>BA, BB, BG, BR, BY, | 20010814<br>BZ. CA. CH. CN. |
|   |                |                                  | DZ, EC, EE, ES, FI,                  |                             |
| GM, HR,                                   |                |                                  | JP, KE, KG, KP, KR,                  |                             |
| · · · · · · · · · · · · · · · · · · ·     |                |                                  | MK, MN, MW, MX, MZ,                  |                             |
| RO, RU,                                   |                |                                  | SL, TJ, TM, TR, TT,                  |                             |
| UZ, VN,                                   |                |                                  |                                      |                             |
|   |                | MW, MZ, SD,                      | SL, SZ, TZ, UG, ZW,                  | AT, BE, CH, CY,             |
|   |                |                                  | IE, IT, LU, MC, NL,                  |                             |
|   |                |                                  | GQ, GW, ML, MR, NE,                  |                             |
| WO 2002016342                             | A1             | 20020228                         | WO 2001-DK542                        | 20010814                    |
| W: AE, AG,                                | AL, AM,        | AT, AU, AZ,                      | BA, BB, BG, BR, BY,                  | BZ, CA, CH, CN,             |
|   |                |                                  | DZ, EC, EE, ES, FI,                  |                             |
| GM, HR,                                   | HU, ID,        | IL, IN, IS,                      | JP, KE, KG, KP, KR,                  | KZ, LC, LK, LR,             |
| LS, LT,                                   |                |                                  | MK, MN, MW, MX, MZ,                  |                             |
| RO, RU,                                   |                |                                  | SL, TJ, TM, TR, TT,                  |                             |
| UZ, VN,                                   | YU, ZA,        |                                  |                                      |                             |
|   |                |                                  | SL, SZ, TZ, UG, ZW,                  |                             |
| DE, DK,                                   | ES, FI,        | FR, GB, GR,                      | IE, IT, LU, MC, NL,                  | PT, SE, TR, BF,             |
| BJ, Cf,                                   | CG, CI,        | CM, GA, GN,                      | GQ, GW, ML, MR, NE,                  | SN, TD, TG                  |
| AU 2001079608                             | A5             | 20020304                         | AU 2001-79608                        | 20010814                    |
| AU 2001079609                             | A5             | 20020304                         |                                      | 20010814                    |
| GR 2001100397                             | A              | 20020524                         | GR 2001-100397                       | 20010814                    |
| GR 1004635                                | B2             | 20040714                         |                                      |                             |
| GR 2001100398                             | Α              | 20020524                         | GR 2001-100398                       | 20010814                    |
| GR 1004074                                | B2             | 20021126                         |                                      |                             |
| ZA 2001006683                             | Α              | 20020805                         | ZA 2001-6683                         | 20010814                    |
| EP 1309581                                | A1             | 20030514                         | EP 2001-957785                       | 20010814                    |
| EP 1309581                                | B1             | 20041103                         |                                      |                             |
|   |                |                                  | GB, GR, IT, LI, LU,                  | NL, SE, MC, PT,             |
|   |                | FI, RO, MK,                      |                                      |                             |
| EP 1309582                                | A1             | 20030514                         | EP 2001-957786                       | 20010814                    |
| EP 1309582                                | B1             | 20041103                         | an an                                |                             |
|   |                |                                  | GB, GR, IT, LI, LU,                  | NL, SE, MC, PT,             |
|   |                | FI, RO, MK,                      |                                      | 20010014                    |
| JP 2004506729                             | T2             |                                  | JP 2002-521442                       | 20010814                    |
| JP 2004506730                             | T2             |                                  | JP 2002-521443                       | 20010814<br>20010814        |
| NZ 523853<br>NZ 523877                    | . A            | 20040730<br>20040827             | NZ 2001-523853<br>NZ 2001-523877     | 20010814                    |
| AT 281447                                 | A<br>E         | 20040827                         | AT 2001-323877                       | 20010814                    |
| AT 281448                                 | E              | 20041115                         | AT 2001-957786                       | 20010814                    |
| PT 1309581                                | T              | 20050331                         | PT 2001-957785                       | 20010814                    |
| PT 1309581<br>PT 1309582                  | T              | 20050331                         | PT 2001-957786                       | 20010814                    |
| ES 2228920                                | <b>T</b> 3     |                                  | ES 2001-1957786                      | 20010014                    |
| ES 2230347                                | T3             |                                  | ES 2001-1957785                      | 20010814                    |
| AU 2001100271                             | A4             |                                  | AU 2001-100271                       | 20010815                    |
| AU 2001100271<br>AU 2001100271            | B4             |                                  | 110 2001 1002/1                      | 20010013                    |
| CZ 294746                                 | B6             |                                  | CZ 2001-2958                         | 20010815                    |
| CZ 295863                                 | · B6           |                                  | CZ 2001-2959                         | 20010815                    |
| AU 2001100278                             | A4             |                                  | AU 2001-100278                       | 20010816                    |
| AU 2001100278                             | B4             |                                  |                                      |                             |
| NL 1018775                                | C1             |                                  | NL 2001-1018775                      | 20010816                    |
| NL 1018776                                | C1             |                                  | NL 2001-1018776                      | 20010816                    |
| BE 1013443                                | A6             |                                  | BE 2001-548                          | 20010816                    |
|   |                |                                  |                                      |                             |

Saloni Sharma 06/19/2006

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FR 2813077
                          Α1
                                 20020222
                                             FR 2001-10855
                                                                     20010816
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     FR 2813077
                          В1
     FR 2813078
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                                 20020222
                                             FR 2001-10857
                                                                     20010816
     FR 2813078
                          В1
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                                             DE 2001-10140028
                                                                     20010816
     DE 10140029
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                                             DE 2001-10140029
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                                             CN 2001-133947
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                                             CN 2001-133948
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                                                                     20010817
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     CN 1515564
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                                             CN 2004-10001871
                          Α
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                          Α
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                                                                     20010820
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                                             BR 2001-5022
                                                                     20010824
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     HK 1047086
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                                             HK 2002-106522
                                                                     20020904
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     BG 107583
                          Α
                                             BG 2003-107583
                                                                     20030224
                                 20040130
     BG 107584
                          Α
                                             BG 2003-107584
                                                                     20030224
PRIORITY APPLN. INFO.:
                                             DK 2000-1231
                                                                  A 20000818
                                             WO 2001-DK541
                                                                     20010814
                                             WO 2001-DK542
                                                                    20010814
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OTHER SOURCE(S):

CASREACT 137:78853

AB Citalopram (I) was prepared by converting a 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran to the 5-carboxylic acid derivative and converting the latter to I. Thus, 5-bromo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran in Me3COMe at -78° was treated with BuLi followed by stirring for 2 h at -30°. Solid CO2 was added followed by stirring for 16 h at room temperature to give 5-carboxy-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran. The latter was heated with sulfamide and SOCl2 in sulfolane at 130° for 2 h to give I.

IT **59729-33-8P**, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of Citalopram from 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of Citalopram from 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

AB Citalopram and other phthalanes I [R1 = CN, R2 = halogen, trifluoromethyl, CN, acyl] are made by treating a salt of I [R1 = halogen] with cuprous cyanide. Thus, 100g I.oxalate [R1 = Br, R2 = F] was treated with 35 g CuCN in diglyme at 150-155° for 3 h to give 35 g I [R1 = CN, R2 = F] as the hydrobromide.

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of phthalanes)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$NC$$
  $O$   $(CH_2)_3 - NMe_2$ 

### HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64372-43-6

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of phthalanes)

RN 64372-43-6 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 64169-39-7 CMF C19 H21 Br F N O

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2002:550142 CAPLUS

DOCUMENT NUMBER:

137:78853

TITLE:

Preparation of Citalopram from 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-

dihydroisobenzofuran.

INVENTOR(S):

Petersen, Hans; Ahmadian, Haleh

PATENT ASSIGNEE(S):

H. Lundbeck A/S, Den.

SOURCE:

Patentschrift (Switz.), 15 pp.

CODEN: SWXXAS

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| CH 691969     | A    | 20011215 | CH 2001-1522    | 20010816 |
| CA 2354880    | AA   | 20020122 | CA 2001-2354880 | 20010809 |
| CA 2354880    | С    | 20030603 |                 |          |
| CA 2354877    | AA   | 20020218 | CA 2001-2354877 | 20010809 |
| CA 2354877    | С    | 20060502 |                 |          |
| FI 2001001621 | A    | 20020219 | FI 2001-1621    | 20010809 |
| FI 2001001622 | A    | 20020219 | FI 2001-1622    | 20010809 |
| IL 144816     | A1   | 20050925 | IL 2001-144816  | 20010809 |
| IT 2001MI1785 | A1   | 20020218 | IT 2001-MI1785  | 20010813 |
| IT 2001MI1786 | A1   | 20020218 | IT 2001-MI1786  | 20010813 |
| IN 194521     | A    | 20041113 | IN 2001-MA665   | 20010813 |
| GB 2362647    | A1   | 20011128 | GB 2001-19733   | 20010814 |
| GB 2362647    | B2   | 20020918 |                 | 4        |
| ZA 2001006687 | Α    | 20020214 | ZA 2001-6687    | 20010814 |
| DK 200101216  | A5   | 20020219 | DK 2001-1216    | 20010814 |
| DK 200101219  | A5   | 20020219 | DK 2001-1219    | 20010814 |
| NO 2001003942 | Α    | 20020219 | NO 2001-3942    | 20010814 |
| NO 2001003943 | Α    | 20020219 | NO 2001-3943    | 20010814 |
| GB 2365865    | A1   | 20020227 | GB 2001-19734   | 20010814 |

ACCESSION NUMBER:

2002:695968 CAPLUS

DOCUMENT NUMBER:

137:216863

TITLE:

Preparation of phthalanes

INVENTOR(S):

Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao;

Rao, Dhanmaraj Ramachandra

PATENT ASSIGNEE(S):

Cipla Ltd., India; Wain, Christopher Paul

SOURCE:

PCT Int. Appl., 11 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

Ι

FAMILY ACC. NUM. COUNT:

| PA       | PATENT NO.           |      |     |                   |  | KIND DATE |      |                |                 |             |        | DATE |     |     |          |      |     |
|----------|----------------------|------|-----|-------------------|--|-----------|------|----------------|-----------------|-------------|--------|------|-----|-----|----------|------|-----|
| WO       | 2002                 |      |     |                   | A1 20020912                            |           |      |                |                 |             |        |      |     |     |          |      |     |
|          | W: AE, AG, AL,       |      |     | , AM, AT, AU, AZ, |  |           | BA,  | BB             | , BG,           | BR,         | BY,    | BZ,  | CA, | CH, | CN,      |      |     |
|          |                      |      |     |                   |  |           |      |                |                 |             | , EE,  |      |     |     |          |      |     |
|          |                      |      |     |                   |  |           |      |                |                 |             | , KG,  |      |     |     |          |      |     |
|          |                      | LS,  | LT, | LU,               | LV,                                    | MA,       | MD,  | MG,            | MK,             | MN          | , MW,  | MX,  | MZ, | NO, | NZ,      | OM,  | PH, |
|          |                      | PL,  | PT, | RO,               | RU,                                    | SD,       | SE,  | SG,            | SI,             | SK          | , SL,  | TJ,  | TM, | TN, | TR,      | TT,  | TZ, |
|          |                      |      |     |                   |  |           | YU,  |                |                 |             |        |      |     |     |          |      |     |
|          | RW:                  | GH,  | GM, | KE,               | LS,                                    | MW,       | MZ,  | SD,            | SL,             | SZ          | , TZ,  | UG,  | ZM, | ZW, | ΑT,      | BE,  | CH, |
|          |                      | CY,  | DE, | DK,               | ES,                                    | FI,       | FR,  | ĠB,            | GR,             | IE,         | , IT,  | LU,  | MC, | NL, | PT,      | SE,  | TR, |
|          |                      | BF,  | ВJ, | CF,               | CG,                                    | CI,       | CM,  | GA,            | GN,             | GQ          | , GW,  | ML,  | MR, | NE, | SN,      | TD,  | TG  |
| CA       | 2442                 |      |     |                   |  |           |      |                | CA 2002-2442613 |             |        |      |     |     |          |      |     |
| EP       | 1366034              |      |     |                   | A1 20031203                            |           |      | EP 2002-702553 |                 |             |        |      |     |     |          |      |     |
|          | R:                   | ΑT,  | ΒĖ, | CH,               | DE,                                    | DK,       | ES,  | FR,            | GB,             | GR          | , IT,  | LI,  | LU, | NL, | SE,      | MC,  | PT, |
|          |                      | ΙE,  | SI, |                   |  |           | RO,  |                |                 |             |        |      |     |     |          |      |     |
| EE       | EE 200300424 '       |      |     | •                 | A 20031215                             |           |      |                |                 | EE 2003-424 |        |      |     |     |          | 0020 | 307 |
|          |                      |      |     |                   |  |           |      | TR 2003-1444   |                 |             |        |      |     |     |          |      |     |
| RU       | 2276                 |      |     |                   |  |           |      |                | RU 2003-129659  |             |        |      |     |     |          |      |     |
| LT       | 5167                 |      |     |                   | В                                      |           |      |                | LT 2003-86      |             |        |      |     |     | 20050550 |      |     |
| BG       | 1082                 | 32   |     |                   | A 20050430                             |           |      | 0430           | BG 2003-108232  |             |        |      |     |     | 20031006 |      |     |
| ГA       | 1313                 | 2    |     |                   | B 20040620                             |           |      | 0620           | LV 2003-107     |             |        |      |     |     | 20031007 |      |     |
| ZA       | 2003                 | 0080 |     |                   | Α                                      |           | 2004 | 1117           | ZA 2003-8039    |             |        |      |     |     | 20031016 |      |     |
| US       | 2004                 | 0927 | 55  |                   | A1                                     |           | 2004 | 0513           |                 | US 2        | 2003-  | 4710 | 52  |     | 2        | 0031 | 118 |
| US       | 6903                 | 228  |     |                   | B2                                     |           | 2005 | 0607           |                 |             |        |      |     |     |          |      |     |
| PRIORIT  | IORITY APPLN. INFO.: |      | .:  |                   |  |           |      |                | GB :            | 2001-       | 5627   |      |     | A 2 | 0010     | 307  |     |
|          |                      |      |     |                   |  |           |      |                |                 |             | 2002-0 |      |     |     | W 2      | 0020 | 307 |
| OTHER SO |                      |      |     |                   | CASREACT 137:216863; MARPAT 137:216863 |           |      |                |                 |             |        |      |     |     |          |      |     |

$$CH_2$$
) 3NMe<sub>2</sub>

$$^{\text{NC}}$$
  $^{\text{O}}$   $^{\text{CH}_2)_3}$   $^{\text{NMe}_2}$ 

• HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

IT 64169-39-7 260066-78-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanation process for the preparation of citalogram from)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 260066-78-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

Bakthavathsalan

PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

|       | PATENT NO. |      |      |      |     | KIND DATE   |     |          | APPLICATION NO. |                 |      |      |      |     | DATE     |          |      |     |  |
|-------|------------|------|------|------|-----|-------------|-----|----------|-----------------|-----------------|------|------|------|-----|----------|----------|------|-----|--|
|       |            |      |      |      |     |             |     |          |                 |                 |      |      |      |     |          |          |      |     |  |
|       | WO         | 2002 | 0725 | 65   |     | A1 20020919 |     |          | WO 2002-IB690   |                 |      |      |      |     | 20020308 |          |      |     |  |
|       |            | W :  | ΑE,  | AG,  | AL, | AM,         | ΑT, | AU,      | ΑZ,             | BA,             | BB,  | ВG,  | BR,  | BY, | ΒZ,      | CA,      | CH,  | CN, |  |
|       |            |      | CO,  | CR,  | CU, | CZ,         | DE, | DK,      | DM,             | DZ,             | EC,  | EE,  | ES,  | FI, | GB,      | GD,      | GE,  | GH, |  |
|       |            |      | GM,  | HR,  | HU, | ID,         | IL, | IN,      | IS,             | JP,             | KE,  | KG,  | ΚP,  | KR, | ΚZ,      | LC,      | LK,  | LR, |  |
|       |            |      | LS,  | LT,  | LU, | LV,         | MA, | MD,      | MG,             | MK,             | MN,  | MW,  | MX,  | ΜZ, | NO,      | NZ,      | OM,  | PH, |  |
|       |            |      | PL,  | PT,  | RO, | RU,         | SD, | SE,      | SG,             | SI,             | SK,  | SL,  | ТJ,  | TM, | TN,      | TR,      | TT,  | TZ, |  |
|       |            |      | UA,  | UG,  | US, | UZ,         | VN, | YU,      | ZA,             | ZM,             | ZW,  | AM,  | AZ,  | BY, | KG,      | KZ,      | MD,  | RU, |  |
|       |            |      | ТJ,  | TM   |     |             |     |          |                 |                 |      |      |      |     |          |          |      |     |  |
|       |            | RW:  | GH,  | GM,  | KE, | LS,         | MW, | ΜZ,      | SD,             | SL,             | SZ,  | TZ,  | UG,  | ZM, | ZW,      | ΑT,      | BE,  | CH, |  |
|       |            |      | CY,  | DE,  | DK, | ES,         | FI, | FR,      | GB,             | GR,             | ΙE,  | ΙT,  | LU,  | MC, | NL,      | PT,      | SE,  | TR, |  |
|       |            |      | BF,  | ВJ,  | CF, | CG,         | CI, | CM,      | GΑ,             | GN,             | GQ,  | GW,  | ML,  | MR, | NE,      | SN,      | TD,  | TG  |  |
|       | CA         | 2439 | 856  |      |     | AA          |     | 2002     | 0919            | CA 2002-2439856 |      |      |      |     | 20020308 |          |      |     |  |
|       | ΕP         | 1370 | 545  |      |     | A1          |     | 2003     | 1217            | EP 2002-702634  |      |      |      |     | 20020308 |          |      |     |  |
|       |            | R:   | ΑT,  | BE,  | CH, | DE,         | DK, | ES,      | FR,             | GB,             | GR,  | IT,  | LI,  | LU, | NL,      | ŞΕ,      | MC,  | PT, |  |
|       |            |      | ΙE,  | SI,  | LT, | LV,         | FI, | RO,      | MK,             | CY,             | AL,  | TR   |      |     |          |          |      |     |  |
|       | CN         | 1496 | 358  |      |     | Α           |     | 2004     | 0512            | CN 20,02-806116 |      |      |      |     | 20020308 |          |      |     |  |
|       | BR         | 2002 | 0078 | 95   |     | Α           |     | 2004     | 1228            | BR 2002-7895    |      |      |      |     |          | 20020308 |      |     |  |
|       | JP         | 2005 | 5002 | 56   |     | T2          |     | 20050106 |                 | JP 2002-571481  |      | 81   |      | 2   | 0020     | 308      |      |     |  |
|       | US         | 2005 | 0855 | 34   |     | A1          |     |          |                 | US 2003-469329  |      |      |      |     |          | 20020308 |      |     |  |
| PRIOF | RITY       | APP  | LN.  | INFO | . : |             |     |          |                 |                 | IN 2 | 001- | DE26 | 4   |          | A 2      | 0010 | 309 |  |
|       |            |      |      |      |     |             |     |          |                 |                 | WO 2 | 002- | IB69 | 0   |          | W 2      | 0020 | 308 |  |
|       |            |      |      |      |     |             |     |          |                 |                 |      |      |      |     |          |          |      |     |  |

# OTHER SOURCE(S): CASREACT 137:232543

- AB An improved and industrially advantageous process for the preparation of citalopram and pharmaceutically acceptable acid addition salts consists of reacting a precursor substituted with a bromo or an iodo group in the same position as the cyano group in citalopram with a cyanide source in a solvent in the present of a N-containing base; the citalopram free base may then be salified with a pharmaceutically acceptable acids.
- IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P,

Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(cyanation process for the preparation of citalogram)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

Saloni Sharma 06/19/2006

ΙT 64372-43-6 479065-02-6

RL: RCT (Reactant); RACT (Reactant or reagent) (process for the preparation of citalogram)

64372-43-6 CAPLUS RN

1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-CN dimethyl-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 64169-39-7 CMF C19 H21 Br F N O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 479065-02-6 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl-, hydrobromide (9CI) (CA INDEX NAME)

● HBr

REFERENCE COUNT:

1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:716262 CAPLUS

DOCUMENT NUMBER: 137:232543

TITLE: Cyanation process for the preparation of citalogram INVENTOR(S): Biswas, Sujay; Sharma, Tarun Kant; Kumar, Yatendra;

Sathyanarayana, Swargam; Vijayaraghavan,

AB An improved process for the preparation of citalopram via substitution of the halogen of halophthalane salts I (R = halogen; X = oxalate, fumarate, maleate, citrate, acetate, formate, hydrochloride, hydrobromide, sulfate) using cuprous cyanide in an organic solvent. Thus, bromophthalane oxalate I (R = Br, X = oxalate) was reacted CuCN in diglyme under a nitrogen atmospheric at

150-155° for 3 h to form citalopram which was converted to its HBr salt I (R = CN, X = HBr).

IT 59729-33-8P, (±)-Citalopram
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN
 (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for the preparation of citalogram)

Ι

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 59729-32-7P,  $(\pm)$ -Citalopram hydrobromide 85118-27-0P,  $(\pm)$ -Citalopram hydrochloride 207559-01-1P,  $(\pm)$ -Citalopram oxalate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of citalogram)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$C$$
 $CH_2)_3-NMe_2$ 
 $F$ 

• HBr

RN 85118-27-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 207559-01-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

A novel method is provided for the manufacture of the antidepressant AB escitalopram, i.e., (S)-I. The method comprises chromatog. separation of the enantiomers of either (1) citalogram, i.e.,  $(\pm)$ -I, or (2) an intermediate in its production, using a chiral stationary phase such as Chiralpak AD or Chiralcel OD. Novel chiral intermediates for the synthesis of escitalopram, made by said method, are also provided. example, the intermediate nitrile diol (±)-II was resolved using Chiralpak AD stationary phase on a Novasep Licosep 10-50 simulated moving bed chromatograph with MeCN mobile phase at 30°, to give both enantiomers of II with purity exceeding 99% ee. Similarly resolved in 96-99% yield and >99% ee were bromide diol (±)-III and bromophthalane (±)-IV, using Chiralpak AD and Chiralcel OD, resp. Resolution of (±)-IV was performed on a 500-g scale using 98:2 isohexane/isopropanol (vol/vol), and also on a smaller scale using supercrit. CO2 with MeOH/Et2NH/CF3CO2H modifier. The obtained bromide (S)-(+)-IV underwent cyanation by Zn(CN)2 and Pd(PPh3)4 according to the method of WO 00/13648, giving escitalopram in 80% yield and 99.6% ee.

IV

IT 488148-14-7P, (S)-(+)-1-(4-Fluorophenyl)-1-[3-

(dimethylamino)propyl]-5-bromophthalane

RL: PUR (Purification or recovery); RCT (Reactant); PREP

(Preparation); RACT (Reactant or reagent)

(intermediate enantiomer; preparation of escitalopram via chromatog. resolution

of citalopram or intermediates using carbohydrate-based chiral stationary phases)

RN 488148-14-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IT 128196-01-0P, Escitalopram

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(preparation of escitalopram via chromatog. resolution of citalopram or intermediates using carbohydrate-based chiral stationary phases)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:8116 CAPLUS

DOCUMENT NUMBER:

138:55857

TITLE:

Process for the preparation of citalogram

INVENTOR(S):

Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao;

Rao, Dharmaraj Ramachandra

PATENT ASSIGNEE(S):

Cipla Limited, India

SOURCE:

Brit. UK Pat. Appl., 11 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1.

PATENT INFORMATION:

| PATENT NO.             | KIND  | DATE          | APPLICATION NO.     | DATE     |  |  |
|------------------------|-------|---------------|---------------------|----------|--|--|
|                        |       |               |                     |          |  |  |
| GB 2376945             | A1    | 20021231      | GB 2001-15708       | 20010627 |  |  |
| PRIORITY APPLN. INFO.: |       |               | GB 2001-15708       | 20010627 |  |  |
| OTHER SOURCE(S):       | CASRE | ACT 138:55857 | 7; MARPAT 138:55857 |          |  |  |

GΙ

CM 2

CRN 64-19-7 CMF C2 H4 O2

IT 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant

or reagent)

(improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7P, 1-(4-Fluorophenyl)-1-(3-dimethylamino-propyl)-5-

bromophthalane

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation and cyanation of; improved process for the manufacture of citalogram

hydrobromide from 5-bromophthalide)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:58074 CAPLUS

DOCUMENT NUMBER:

138:122548

TITLE:

Method for the preparation of escitalopram via chromatographic resolution of citalopram or its intermediates using carbohydrate-based chiral

stationary phases

INVENTOR(S):

Bech Sommer, Michael; Nielsen, Ole; Petersen, Hans; Ahmadian, Haleh; Pedersen, Henrik; Brosen, Peter; Geiser, Fiona; Lee, James; Cox, Geoffey; Dapremont, Olivier; Suteu, Christina; Assenza, Sebastian P.;

Hariharan, Shankar; Nair, Usha

PATENT ASSIGNEE(S):

SOURCE:

H. Lundbeck A/S, Den.

PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

OTHER SOURCE(S):

GI

| PA     | PATENT NO. |      |      |     |             | KIND DATE |                 |                |               | APPL | ICAT     |      |          |          |          |      |      |  |
|--------|------------|------|------|-----|-------------|-----------|-----------------|----------------|---------------|------|----------|------|----------|----------|----------|------|------|--|
| WO     | 2003       | 0064 | 49   |     | A1 20030123 |           |                 | 1              | 002-          | DK49 |          |      |          |          |          |      |      |  |
|        | W:         | ΑE,  | AG,  | AL, | AM,         | ΑT,       | AU,             | AZ,            | BA,           | BB,  | BG,      | BR,  | BY,      | ΒZ,      | CA,      | CH,  | CN,  |  |
|        |            | CO,  | CR,  | CU, | CZ,         | DE,       | DK,             | DM,            | DZ,           | EC,  | EE,      | ES,  | FI,      | GB,      | GD,      | GE,  | GH,  |  |
|        |            |      |      |     |             |           |                 |                |               |      | KG,      |      |          |          |          |      |      |  |
|        |            | LS,  | LT,  | LU, | LV,         | MA,       | MD,             | MG,            | MK,           | MN,  | MW,      | MX,  | MZ,      | NO,      | NZ,      | OM,  | PH,  |  |
|        |            |      |      |     |             |           |                 |                |               |      | SL,      |      |          |          |          |      |      |  |
|        |            | UΑ,  | UG,  | US, | UΖ,         | VN,       | YU,             | ZA,            | ZM,           | zw   |          |      |          |          |          |      |      |  |
|        | RW:        | GH,  | GM,  | ΚE, | LS,         | MW,       | MZ,             | SD,            | SL,           | SZ,  | TZ,      | UG,  | ZM,      | ZW,      | AT,      | BE,  | BG⁻, |  |
|        |            | CH,  | CY,  | CZ, | DE,         | DK,       | EE,             | ES,            | FI,           | FR,  | GB,      | GR,  | IE,      | IT,      | LU,      | MC,  | NL,  |  |
|        |            | PT,  | SE,  | SK, | TR,         | BF,       | ВJ,             | CF,            | CG,           | CI,  | CM,      | GA,  | GN,      | GQ,      | GW,      | ML,  | MR,  |  |
|        |            | NE,  | SN,  | TD, | TG          |           |                 |                |               |      |          |      |          |          |          |      |      |  |
| CA     | 2451       | 124  |      |     | AA 20030123 |           | CA 2002-2451124 |                |               |      |          |      | 20020712 |          |          |      |      |  |
| EP     | 1409       | 472  |      |     | A1 20040421 |           | 0421            | EP 2002-750836 |               |      |          |      |          | 20020712 |          |      |      |  |
|        | R:         | ΑT,  | BE,  | CH, | DE,         | DK,       | ES,             | FR,            | GB,           | GR,  | IT,      | LI,  | LU,      | NL,      | SE,      | MC,  | PT,  |  |
|        |            | ΙE,  | SI,  | LT, | LV,         | FI,       | RO,             | MK,            | CY,           | ΑL,  | TR,      | BG,  | CZ,      | EE,      | SK       |      |      |  |
| BR     | 2002       | 0108 | 17   |     | Α           |           | 2004            | 0622           | BR 2002-10817 |      |          |      |          |          | 20020712 |      |      |  |
| CN     | 1527       | 825  |      |     | A 20040908  |           | CN 2002-813998  |                |               |      |          |      | 20020712 |          |          |      |      |  |
|        | 2004       |      | 76   |     | T2 20041224 |           | JP 2003-512221  |                |               |      | 20020712 |      |          |          |          |      |      |  |
| ZA     | 2003       | 0094 | 71   |     | Α           |           | 2004            | 1206           |               | ZA 2 | 003-     | 9471 |          |          | 2        | 0031 | 205  |  |
| BG     | 1085       | 72   |      |     | Α           |           | 2005            | 0331           |               | BG 2 | 004-     | 1085 | 72       |          | 2        | 0040 | 209  |  |
| US     | 2005       | 0652 | 07   |     | A1          |           | 2005            | 0324           | •             | US 2 | 004-     | 4838 | 24       |          | 2        | 0040 | 930  |  |
| RIORIT | Y APP      | LN.  | INFO | .:  |             |           |                 |                |               | DK 2 | 001-     | 1101 |          |          | A 2      | 0010 | 713  |  |
|        |            |      |      |     |             |           |                 |                |               | DK 2 | 001-     | 1851 |          |          | A 2      | 0011 | 211  |  |
|        |            |      |      |     |             |           |                 |                |               | DK 2 | 001-     | 1852 |          |          | A 2      | 0011 | 211  |  |
|        |            |      |      |     |             |           |                 |                | ,             | WO 2 | 002-     | DK49 | 1        |          | W 2      | 0020 | 712  |  |

CASREACT 138:122548

Saloni Sharma 06/19/2006

#### HBr

RN 207559-01-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 500733-84-6 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.:

US 2001-315391P P 20010828
OTHER SOURCE(S):

CASREACT 138:221462; MARPAT 138:221462
GI

$$\begin{array}{c|c} w_n & & w_n \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & \\ & & \\ & & \\ & \\ & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\$$

AB A process for the preparation of 1-(4'-fluorophenyl)-1-(3-dimethylamino-propyl)-

5-phthalanecarbonitrile (I), or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields. Also claimed is a process for the preparation of aryl ketone II [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl, optionally containing one heteroatom; W = haloge, CN, OH, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl; n = 0 - 4] which comprises the step of reacting a phthalide III with a Grignard reagent, R1MgY (Y = halogen) and is characetrized in that the phthalide is reacted with a Lewis acid to form an adduct prior to reaction with the Grignard reagent. Thus,.

59729-32-7P, Citalopram hydrobromide 207559-01-1P, Citalopram oxalate 500733-84-6P; Citalopram acetate RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(improved process for the manufacture of citalogram hydrobromide from 5-bromophthalide)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

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MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                              CA 1999-2353618
     CA 2353618
                           AA
                                  20000615
                                              BR 1999-16873
     BR 9916873
                           Α
                                  20010821
                                                                       19991203
                                              EP 1999-957263
     EP 1137644
                           A1
                                  20011004
                                                                       19991203
     EP 1137644
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         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     TR 200101605
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                           A1
                                                                       19991203
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     US 2002032205
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     NO 2001002802
                           Α
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                                  20020228
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     BG 105646
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                                  20051216
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PRIORITY APPLN. INFO.:
                                              US 1998-111360P
                                                                    Ρ
                                                                       19981208
                                               DK 1998-1631
                                                                    Α
                                                                       19981209
                                               WO 1999-DK676
                                                                    W
                                                                       19991203
                                                                    Α
                                               US 2000-632117
                                                                       20000803
                                               WO 2001-US23487
                                                                    A 20010726
OTHER SOURCE(S):
                         MARPAT 133:43427
```

#### \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compds. [I; R1 = H, halo, CF3, etc.; R2, R3 = H, CF3, alkyl, etc.; n = 1-5; m = 0-1; A = N(R4)DsZq, II-IV (wherein Z = O, S; s = 0-1; q = 0-1; R4 = H, alkyl, alkenyl, etc.; D = alkylene, alkenylene, alkynylene); B = (un)substituted Ph, indolyl, etc.; Ar = (un)substituted Ph, thienyl, furanyl, etc.] and their pharmaceutically acceptable acid addition salts which are potently binding to the 5-HT1A receptor, were prepared Thus, reacting 5-(4-bromobutyl)-1,4-benzodioxane (preparation given) with (+)-1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile in the presence of K2CO3 in Me iso-Bu ketone afforded 73% (+)-V which showed IC50 of 39 nM against 3H-5-CT binding and IC50 of 60 nM against serotonin reuptake.

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TT 274908-99-5P 274909-01-2P 274909-03-4P 274909-05-6P 274909-07-8P 274909-08-9P 274909-09-0P 274909-11-4P 274909-17-0P 274909-26-1P 274909-24-9P 274909-25-0P 274909-26-1P 274909-30-7P 274909-31-8P 274909-32-9P 274909-33-0P 274909-34-1P 274909-35-2P 274909-36-3P 274909-37-4P 274909-38-5P 274909-39-6P 274909-40-9P 274909-41-0P 274909-42-1P 274909-43-2P
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halophthalane in the corresponding Grignard reagent; this intermediate product may be converted into citalopram via intermediate formation of an aldehyde and in the subsequent transformation of the functional group via oxime or hydrazone; or else be converted into citalopram via reaction with compds. containing a cyano group bound to a leaving group. The process described makes it possible to obtain citalopram in high yields, and does not involve the use of drastic conditions of temperature 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); PREP (Preparation) (process for synthesis of citalogram)

RN 59729-33-8 CAPLUS

IT

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7D, Grignard compound

RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for synthesis of citalogram)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2000:401811 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

133:43427

TITLE:

Preparation of benzofurans as 5-HT1A receptor ligands Andersen, Kim; Rottlander, Mario; Bogeso, Klaus Peter; Pedersen, Henrik; Ruhland, Thomas; Dancer, Robert

PATENT ASSIGNEE(S):

H. Lundbeck A/S, Den.

SOURCE:

PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO.    |     |     | KIN | D   | DATE      |     |      | APPL          | ICAT: | DATE |     |     |     |          |     |     |
|---------------|-----|-----|-----|-----|-----------|-----|------|---------------|-------|------|-----|-----|-----|----------|-----|-----|
|               |     |     |     |     | -         |     |      |               |       |      |     |     |     |          |     |     |
| WO 2000034263 |     |     |     | A1  | A1 200006 |     | 0615 | WO 1999-DK676 |       |      |     |     |     | 19991203 |     |     |
| ₩:            | ΑE, | AL, | AM, | AT, | AU,       | AZ, | BA,  | BB,           | BG,   | BR,  | BY, | CA, | CH, | CN,      | CU, | CZ, |
|               | DE, | DK, | EE, | ES, | FI,       | GB, | GD,  | GE,           | GH,   | GM,  | HR, | HU, | ID, | IL,      | IN, | ıs, |
|               | JP, | ΚĒ, | KG, | KP, | KR,       | ΚZ, | LC,  | LK,           | LR,   | LS,  | LT, | LU, | LV, | MD,      | MG, | MK, |

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274909-44-3P 274909-45-4P 274909-48-7P
     274909-49-8P 274909-50-1P 274909-51-2P
     274909-52-3P 274909-53-4P 274909-54-5P
     274909-55-6P 274909-57-8P 274909-58-9P
     274909-59-0P 274909-60-3P 274909-61-4P
     274909-62-5P 274909-63-6P 274909-64-7P
     274909-65-8P 274909-66-9P 274909-67-0P
     274909-68-1P 274909-69-2P 274909-70-5P
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     274909-99-8P 274910-00-8P 274910-01-9P
     274910-02-0P 274910-03-1P 274910-04-2P
     274910-05-3P 274910-06-4P 274910-07-5P
     274910-08-6P 274910-09-7P 274910-10-0P
     274910-11-1P 274910-12-2P 274910-13-3P
     274910-15-5P 274910-17-7P 274910-52-0P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation);
     USES (Uses)
        (preparation of benzofurans as 5-HT1A receptor ligands)
RN
     274908-99-5 CAPLUS
CN
     5-Isobenzofurancarbonitrile, 1-[3-[[4-(2,3-dihydro-1,4-benzodioxin-5-
     yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI)
     (CA INDEX NAME)
```

Absolute stereochemistry. Rotation (+).

NC 
$$Me$$
  $(CH_2)_4$   $(CH_2)_4$ 

```
RN 274909-01-2 CAPLUS

5-Isobenzofurancarbonitrile, 1-[3-[[3-(2,3-dihydro-1,4-benzodioxin-5-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274909-00-1
```

Absolute stereochemistry.

C30 H31 F N2 O3

CMF

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274909-03-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(2,3-dihydro-1,4-benzodioxin-5-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274909-02-3 CMF C29 H29 F N2 O3

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274909-05-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[(2,3-dihydro-1,4-benzodioxin-5-yl)methyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274909-04-5 CMF C28 H27 F N2 O3

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274909-07-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(2-methoxyphenoxy)ethyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{NC} & \text{Me} \\ \hline \\ \text{O} & \text{(CH}_2)_3 - \text{N-CH}_2 - \text{CH}_2 - \text{O} \\ \hline \\ \text{F} \end{array}$$

RN 274909-08-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(3-methoxyphenoxy)ethyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} \\ \hline \\ \text{(CH}_2)_3 - \text{N-CH}_2 - \text{CH}_2 - \text{O} \\ \hline \\ & \text{F} \end{array}$$

RN 274909-09-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[4-(1H-indol-3-yl)butyl]methylamino]propyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_{4}^{H}$$

$$(CH_2)_{3}^{O}$$

$$F$$

RN 274909-11-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl]methylamino]propyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 274909-17-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-chlorophenyl)-1-[3-[[3-(2,3-dihydro-1,4-benzodioxin-5-yl)propyl]methylamino]propyl]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274909-23-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(1H-indol-3-yl)ethyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 274909-24-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(3-

methoxyphenyl)ethyl]methylamino]propyl] - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} \\ \hline \\ \text{(CH}_2)_3 - \text{N-CH}_2 - \text{CH}_2 \\ \hline \\ \end{array} \\ \text{OMe}$$

RN 274909-25-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, '1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(3-methoxyphenyl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{NC} & \text{CH}_2\text{-}\text{CH} = \text{CH}_2 \\ \hline \\ \text{(CH}_2)_3\text{-}\text{N} - \text{CH}_2\text{-}\text{CH}_2 \\ \hline \\ \text{F} \end{array}$$

RN 274909-26-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(2-methoxyphenyl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC 
$$CH_2$$
—  $CH_2$ —  $C$ 

RN 274909-27-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(2,5-dimethoxyphenyl)ethyl]methylami no]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

NC Me (CH<sub>2</sub>) 
$$_3$$
 N - CH<sub>2</sub> - CH<sub>2</sub> OMe

RN 274909-28-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(2,5-dimethoxyphenyl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

NC 
$$CH_2-CH$$
  $CH_2$   $C$ 

RN 274909-29-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl(2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-30-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(1H-indol-3-yl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$
 $CH_2 - CH_2 - N - (CH_2)_3$ 
 $CN$ 

RN 274909-31-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[(2-phenoxyethyl)-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-32-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenyl)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

NC Me MeO (
$$CH_2$$
)  $_3-N-$  ( $CH_2$ )  $_3$ 

RN 274909-33-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenyl)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC 
$$CH_2-CH=CH_2$$
  $CH_2$   $CH_$ 

RN 274909-34-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(3-methoxyphenyl)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC 
$$CH_2-CH$$
  $CH_2$   $C$ 

RN 274909-35-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenoxy)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

NC Me MeO (CH<sub>2</sub>) 
$$_3$$
 N- (CH<sub>2</sub>)  $_3$  - O

RN 274909-36-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenoxy)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC 
$$CH_2-CH=CH_2$$
  $CH_2$   $CH_$ 

RN 274909-37-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(3-methoxyphenoxy)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} \\ & \text{O} \\ & \text{CH}_2)_3 - \text{N-} \\ & \text{CH}_2)_3 - \text{O} \\ \end{array}$$

RN 274909-38-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(3-methoxyphenoxy)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC 
$$CH_2-CH=CH_2$$
  $CH_2$   $CH_$ 

RN 274909-39-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[2-(phenylmethoxy)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-40-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(phenylmethoxy)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-41-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-

indol-3-yl)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274909-42-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$
 $CH_2$ 
 $H_3 = CH - CH_2$ 
 $H_4 = CH_4$ 
 $H_4 = CH_4$ 

RN 274909-43-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl]-2-propynylamino]propyl]- (9CI) (CA INDEX NAME)

HC 
$$\equiv$$
 C-CH<sub>2</sub>

(CH<sub>2</sub>)<sub>3</sub>-N-(CH<sub>2</sub>)<sub>3</sub>

CN

RN 274909-44-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[2-(5-methyl-1H-indol-3-yl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

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Me 
$$CH_2-CH_2-N-(CH_2)_3$$
  $CN$ 

RN 274909-45-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(7-fluoro-1H-indol-3-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
\text{Me} \\
\text{CH}_2 - \text{CH}_2 - \text{N} - (\text{CH}_2)_3 \\
\text{O}
\end{array}$$
CN

RN 274909-48-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[3-(5-methyl-1H-indol-3-yl)propyl]amino]propyl]- (9CI) (CA INDEX NAME)

Me (CH<sub>2</sub>) 3 - N - (CH<sub>2</sub>) 3 
$$\stackrel{\text{Me}}{\longrightarrow}$$
 CN

RN 274909-49-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-50-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(5-methyl-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Me
$$CH_2-CH_2-N-(CH_2)_3$$
 $N$ 
 $H$ 
 $CH_2-CH_2-N-(CH_2)_3$ 

RN 274909-51-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(7-fluoro-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274909-52-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-fluoro-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274909-53-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(5-fluoro-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

F

$$CH_2-CH_2-N-(CH_2)_3$$
 $N$ 
 $H$ 
 $CH_2-CH_2-N-(CH_2)_3$ 
 $CN$ 

RN 274909-54-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(7-fluoro-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX

$$\begin{array}{c|c}
Et \\
CH_2-CH_2-N-(CH_2)_3
\end{array}$$
CN

RN 274909-55-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-chloro-1H-indol-3-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CAINDEX NAME)

C1

$$Me$$
 $CH_2-CH_2-N-(CH_2)_3$ 
 $CN$ 

RN 274909-57-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[4-(5-methyl-1H-indol-3-yl)butyl]amino]propyl]- (9CI) (CA INDEX NAME)

Me 
$$(CH_2)_4 - N - (CH_2)_3$$
  $CN$ 

RN 274909-58-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(5-methyl-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Me (CH<sub>2</sub>)<sub>3</sub>-N-(CH<sub>2</sub>)<sub>3</sub>

$$\stackrel{\text{Et}}{\underset{\text{H}}{\bigvee}}$$
 $\stackrel{\text{CN}}{\underset{\text{CN}}{\bigvee}}$ 

RN 274909-59-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(7-fluoro-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & \text{Et} \\
 & \text{CH}_2)_3 - \text{N} - (\text{CH}_2)_3
\end{array}$$
CN

RN 274909-60-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(5-fluoro-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-61-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-chloro-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-62-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(7-chloro-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CFINDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \hline \\ & & \\ &$$

RN 274909-63-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-chloro-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1 \xrightarrow{\text{Et}} CH_2 - CH_2 - N - (CH_2)_3 \xrightarrow{\text{CN}} CN$$

RN 274909-64-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

F

$$CH_2-CH_2-N-(CH_2)_3$$
 $CN$ 

RN 274909-65-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[4-(5-fluoro-1H-indol-3-yl)butyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-66-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[4-(5-chloro-1H-indol-3-yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1

Me

(CH<sub>2</sub>) 
$$_4$$

N

H

(CH<sub>2</sub>)  $_4$ 

(CH<sub>2</sub>)  $_3$ 

(CN

CN

RN 274909-67-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-chloro-1H-indol-3-yl)propyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1

$$(CH_2)_3 - N - (CH_2)_3$$
 $N$ 
 $H$ 

RN 274909-68-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5,7-difluoro-1H-indol-3-yl)propyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CIINDEX NAME)

(CA

F

$$(CH_2)_3$$
 $(CH_2)_3$ 
 $(CH_2)_3$ 
 $(CH_2)_3$ 
 $(CH_2)_3$ 
 $(CH_2)_3$ 

INDEX NAME)

RN 274909-69-2 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI)

Br  $CH_2-CH_2-N-(CH_2)_3$  CN

RN 274909-70-5 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-bromo-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Br  $(CH_2)_3 - N - (CH_2)_3$ 

RN 274909-71-6 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

Saloni Sharma 06/19/2006

Br 
$$CH_2-CH_2-N-(CH_2)_3$$
  $CN$ 

RN 274909-72-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[4-(5-bromo-1H-indol-3-yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CAINDEX NAME)

Br 
$$(CH_2)_4 - N - (CH_2)_3$$
  $CN$ 

RN 274909-73-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-bromo-1H-indol-3-yl)propyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

Br 
$$(CH_2)_3$$
  $N$   $(CH_2)_3$   $O$   $CN$ 

RN 274909-74-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(5-iodo-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Et} \\ \text{CH}_2 - \text{CH}_2 - \text{N} - \text{(CH}_2)_3 \end{array}$$

RN 274909-75-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(5-iodo-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-76-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[2-[[4-(5-chloro-1H-indol-3-yl)butyl]methylamino]ethyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1
$$(CH_2)_4 - N - CH_2 - CH_2$$

$$CN$$

$$CN$$

RN 274909-77-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

F

$$CH_2-CH_2-N-(CH_2)_4$$
 $CH_2$ 
 $CN$ 

RN 274909-78-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-{4-[[2-(7-chloro-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 274909-79-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(5-chloro-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274909-80-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(5-bromo-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

Br 
$$CH_2-CH_2-N-(CH_2)_4$$
  $CN$ 

RN 274909-81-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[4-[methyl[2-(5-methyl-1H-indol-3-yl)ethyl]amino]butyl]- (9CI) (CA INDEX NAME)

Me 
$$CH_2-CH_2-N-(CH_2)_4$$
  $CN$ 

RN 274909-82-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[4-[[2-(5-iodo-1H-indol-3-yl)ethyl]methylamino]butyl]- (9CI) (CA INDEX NAME)

I 
$$CH_2-CH_2-N-(CH_2)_4$$
  $CN$ 

RN 274909-83-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-[5-(1,1-dimethylethyl)-1H-indol-3-yl]ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

t-Bu 
$$CH_2-CH_2-N-(CH_2)_4$$
  $CN$ 

RN 274909-84-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[4-[methyl[2-[5-(1-methylethyl)-1H-indol-3-yl]ethyl]amino]butyl]- (9CI) (CA INDEX NAME)

i-Pr 
$$CH_2-CH_2-N-(CH_2)_4$$
  $CN$ 

RN 274909-85-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(5-methyl-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{H}_2\text{C} = \text{CH} - \text{CH}_2 \\ \text{Me} \\ \text{CH}_2 - \text{CH}_2 - \text{N} - (\text{CH}_2)_3 \\ \text{N} \\ \text{H} \end{array}$$

RN 274909-87-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-fluoro-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_{2}C = CH - CH_{2}$$

$$CH_{2} - CH_{2} - N - (CH_{2})_{3}$$

$$N$$

$$H$$

RN 274909-89-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(7-fluoro-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$H_{2}C = CH - CH_{2}$$

$$CH_{2} - CH_{2} - N - (CH_{2})_{3}$$

$$CN$$

RN 274909-91-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-fluoro-1H-indol-3-y1)propy1]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & &$$

RN 274909-93-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(7-fluoro-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274909-94-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-chloro-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{C1} \\ \text{H}_2\text{C} = \text{CH} - \text{CH}_2 \\ \text{CH}_2 - \text{CH}_2 - \text{N} - (\text{CH}_2)_3 \end{array}$$

RN 274909-95-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl]propylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

F

$$CH_2-CH_2-N-(CH_2)_3$$
 $CN$ 
 $CN$ 

RN 274909-96-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[(1-methylethyl)[2-[5-(1-methylethyl)-1H-indol-3-yl]ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-97-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(4-fluoro-7-methyl-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-98-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(4-chloro-7-methyl-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

C1 
$$H_2C = CH - CH_2$$
  $CH_2 - CH_2 - N - (CH_2)_3$   $CN$ 

RN 274909-99-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-chloro-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

C1

$$H_2C = CH - CH_2$$
 $CH_2)_3 - N - (CH_2)_3$ 
 $CN$ 

RN 274910-00-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[2-propenyl[2-(1H-pyrrolo[3,2-h]quinolin-3-yl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

RN 274910-01-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(7-fluoro-1H-indol-3-yl)propyl](2-furanylmethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274910-02-0 CAPLUS

CN 1H-Indole-7-carboxylic acid, 3-[4-[[3-[5-cyano-1-(4-fluorophenyl)-1,3-dihydro-1-isobenzofuranyl]propyl]-2-propenylamino]butyl]- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$

$$(CH_2)_4 - N - (CH_2)_3$$

$$CO_2H$$

$$CO_2H$$

RN 274910-03-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl]propylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Br 
$$CH_2-CH_2-N-(CH_2)_3$$
  $CN$ 

RN 274910-04-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 274910-05-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(5-methyl-1H-indol-3-yl)ethyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{PhO-CH}_2\text{-CH}_2\\ \text{Me} \\ \text{CH}_2\text{-CH}_2\text{-N-(CH}_2)_3 \\ \text{N} \\ \text{H} \end{array}$$

RN 274910-06-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-fluoro-1H-indol-3-yl)ethyl](2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

RN 274910-07-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1-[3-[(2-furanylmethyl)[3-(1H-pyrrolo[3,2-h]quinolin-3-yl)propyl]amino]propyl]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274910-08-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(5-methyl-1H-indol-3-yl)propyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

Me

Pho-CH<sub>2</sub>-CH<sub>2</sub>

$$(CH_2)_3$$
-N-  $(CH_2)_3$ 
 $(CH_2)_3$ -N-  $(CH_2)_3$ 
 $(CH_2)_3$ -N-  $(CH_2)_3$ 

RN 274910-09-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-fluoro-1H-indol-3-yl)propyl] (2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

RN 274910-10-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl](2-phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274910-11-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1-[3-[(2-furanylmethyl)[4-(1H-pyrrolo[3,2-h]quinolin-3-yl)butyl]amino]propyl]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274910-12-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-[5-(1-methylethyl)-1H-indol-3-yl]ethyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

RN 274910-13-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl](2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

$$\begin{array}{c} \text{PhO-CH}_2\text{-CH}_2\\ \text{CH}_2\text{-CH}_2\text{-N-(CH}_2)_3\\ \text{N}\\ \text{H} \end{array}$$

RN 274910-15-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[4-(2,3-dihydro-1,4-benzodioxin-5-yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 274910-17-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(2,3-dihydro-1,4-benzodioxin-5-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274910-16-6 CMF C30 H31 F N2 O3

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274910-52-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[2-[[4-(5-bromo-1H-indol-3-yl)butyl]methylamino]ethyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA

INDEX NAME)

Br 
$$(CH_2)_4 - N - CH_2 - CH_2$$
  $CN$ 

IT 274910-18-8P

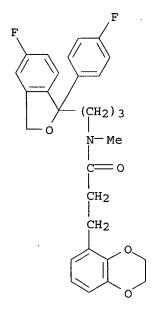
RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of benzofurans as 5-HT1A receptor ligands)

RN 274910-18-8 CAPLUS

CN 1,4-Benzodioxin-5-propanamide, N-[3-[5-fluoro-1-(4-fluorophenyl)-1,3-dihydro-1-isobenzofuranyl]propyl]-2,3-dihydro-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:175646 CAPLUS

DOCUMENT NUMBER: 132:194283

TITLE: Method for the preparation of citalopram

INVENTOR(S): Petersen, Hans; Rock, Michael Harold; Svane, Henrik

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den. SOURCE: PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

2

LANGUAGE:
FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO.                                   |               | KIN       | D DATE               | APPLICATION NO.                 | DATE                 |  |  |
|--|---------------|-----------|----------------------|---------------------------------|----------------------|--|--|
| WO 2000013648<br>WO 2000013648               | 3<br>3        | A2<br>A3  | 20000316<br>20000713 | WO 1999-DK640                   | 19991122             |  |  |
|  |               |           |                      | BB, BG, BR, BY, CA, CH          |                      |  |  |
|  |               |           |                      | GE, GH, GM, HR, HU, ID          |                      |  |  |
| JP, I  | KE, KG,       | ΚP,       | KR, KZ, LC,          | LK, LR, LS, LT, LU, LV          | , MD, MG, MK,        |  |  |
|  |               |           |                      | RO, RU, SD, SE, SG, SI          | , SK, SL, TJ,        |  |  |
|  |               |           |                      | VN, YU, ZA, ZW                  |                      |  |  |
|  |               |           |                      | SZ, TZ, UG, ZW, AT, BE          |                      |  |  |
| DK, I  | ES, FI,       | FR,       | GB, GR, IE,          | IT, LU, MC, NL, PT, SE          | , BF, BJ, CF,        |  |  |
|  | CI, CM,       | GA,       | GN, GW, ML,          | MR, NE, SN, TD, TG              |                      |  |  |
| IT 99MI1581                                  |               | A1        | 20010115             | IT 1999-MI1581<br>ES 2001-50056 | 19990715             |  |  |
|  | ES 2169709    |           | 20020701             | ES 2001-50056                   | 19991025             |  |  |
|  |               |           |                      | JP 2002-106016                  |                      |  |  |
| EP 1298124                                   | טוס פונ       | A1        |                      | EP 2002-28326                   |                      |  |  |
| K: Al, I                                     | er, en,       | DE,       | FI, RO, MK,          | GB, GR, IT, LI, LU, NL          | , SE, MC, PT,        |  |  |
| CN 1550497                                   |               |           | 20041201             | CN 2003-2003165033              | 10001005             |  |  |
|  |               |           |                      | AU 2000-13745                   |                      |  |  |
| CA 2290127                                   | ,             | 77        | 20000327             | CA 1999-2290127                 |                      |  |  |
| CA 2290127<br>CA 2290127                     | . ,           | ر.<br>دير | 20051225             | CR 1999-2290127                 | 19991122             |  |  |
| CA 2475401                                   |               | ΔΔ        | 20030125             | CA 1999-2475401                 | 19991122             |  |  |
|  |               |           | _                    | GB 2001-1504                    | 19991122             |  |  |
| GB 2354239                                   |               | B2        | 20010606             | 05 2001 2001                    | 17771122             |  |  |
| GB 2357761                                   |               | B2<br>A1  | 20010704             | GB 2001-5182                    | 19991122             |  |  |
| GB 2357761                                   |               | B2        | 20010905             |                                 | 2,7,7,2,2,0          |  |  |
| AU 2001100440                                |               | <b>A4</b> | 2221121              | AU 2001-2001100440              | 19991122             |  |  |
| AU 2001100440<br>AU 2001100440               |               | B4        | 20020124             |                                 |                      |  |  |
| EP 1159274                                   |               | A2        | 20011205             | EP 1999-968622                  | 19991122             |  |  |
| EP 1159274                                   |               | B1        | 20030326             |                                 | •                    |  |  |
|  |               |           |                      | GB, GR, IT, LI, LU, NL          | , SE, MC, PT,        |  |  |
|  | SI, LT,       | LV,       | FI, RO               |                                 |                      |  |  |
| BR 9917368                                   |               | Α         | 20020305             | BR 1999-17368<br>AT 1999-9041   | 19991122             |  |  |
| AT 9909041                                   |               | Α         | 20020515             | AT 1999-9041                    | 19991122             |  |  |
| AT 409961                                    |               | В         | 20021227             |                                 |                      |  |  |
| TR 200103702<br>DE 19983487<br>JP 2002526386 |               | T2        | 20020621             | TR 2001-200103702               |                      |  |  |
| DE 1998348/                                  | =             | CI        | 20020725<br>20020820 | DE 1999-19983487                | 19991122             |  |  |
| JP 3447267                                   | •             | 12        | 20020820             | JP 2000-568457                  | 19991122             |  |  |
| AT 235478                                    |               | E<br>E    | 20030916             | AT 1999-968622                  | 10001100             |  |  |
| ES 2189699                                   |               | A1        |                      | ES 2001-50011                   |                      |  |  |
| CZ 292198                                    |               | B6        | 20030701             | CZ 2001-30011                   | 19991122<br>19991122 |  |  |
| PT 1159274                                   |               | T         | 20030813             | PT 1999-968622                  | 19991122             |  |  |
| ES 2194545                                   |               | Т3        | 200311116            | ES 1999-968622                  | 19991122             |  |  |
| NZ 514979                                    |               |           | 20040130             | NZ 1999-514979                  | 19991122             |  |  |
| CN 1502616                                   |               |           | 20040609             | CN 2003-10118780                | 19991122             |  |  |
| SE 2001000193                                |               |           | 20010425             | SE 2001-193                     | 20010124             |  |  |
| SE 516690                                    |               |           | 20020212             | <del></del>                     |                      |  |  |
| FI 2001000155                                |               | Α         | 20010209             | FI 2001-155                     | 20010125             |  |  |
| FI 108641                                    |               |           | 20020228             |                                 |                      |  |  |
| ZA 2001008854                                | ZA 2001008854 |           | 20020611             | ZA 2001-8854                    | 20011026             |  |  |
| US 2002077353                                | 3             | A1        | 20020620             | US 2001-12054                   | 20011106             |  |  |
| BG 106191                                    | 3G 106191     |           | 20020830             | BG 2001-106191                  | 20011207             |  |  |

## Qazi 10/500,532 Page 112

| HK 1049002             | A1     | 20041231    | HK | 2003-101234  |            | 20030218 |
|------------------------|--------|-------------|----|--------------|------------|----------|
| PRIORITY APPLN. INFO.: |        |             | DK | 1999-920     | Α          | 19990625 |
|                        |        |             | EP | 1999-950511  | <b>A</b> 3 | 19991025 |
|                        |        |             | JP | 2000-571018  | Α3         | 19991025 |
|                        |        |             | CA | 1999-2290127 | <b>A</b> 3 | 19991122 |
|                        |        |             | CN | 1999-816751  | Α          | 19991122 |
|                        |        |             | GB | 2001-1504    | <b>A</b> 3 | 19991122 |
|                        |        |             | WO | 1999-DK640   | W          | 19991122 |
| 6 mil m                | ~~ ~~~ | OT 130 1040 |    |              |            |          |

OTHER SOURCE(S):

CASREACT 132:194283; MARPAT 132:194283

ĢΙ

AB The title compound [I; R = CN], the well known antidepressant (no data), was prepared by reacting a compound I [wherein R = halo, CF3(CF2)nSO2; n = 0-8] with a cyanide source in the presence of a palladium catalyst and a catalytic amount of Cu+ or Zn2+, or with Zn(CN)2 in the presence of a palladium catalyst.

IT 59729-33-8P, Citalopram 207559-01-1P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method for the preparation of citalogram)

Ι

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

Saloni Sharma 06/19/2006

CM 2

CRN 144-62-7 CMF C2 H2 O4

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent) (method for the preparation of citalogram)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

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